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INBREEDING AND LITTER SIZE IN SIXTEEN CONTROL POPULATIONS OF MICE OF DIFFERENT ORIGINS

by

© *ABDOLHOSSAIN FARID-NAEINI*

A THESIS
SUBMITTED TO THE FACULTY OF GRADUATE STUDIES AND RESEARCH
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OF *DOCTOR OF PHILOSOPHY*
IN
ANIMAL BREEDING AND GENETICS

DEPARTMENT OF ANIMAL SCIENCE

EDMONTON, ALBERTA
SPRING 1986

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DEDICATION

To the Memory of My Father

Alireza Farid-Naeini

ABSTRACT

The theoretical rate of inbreeding for a cyclical mating system in which one male and one female were selected from each of the n families per generation (population size N=2n), and males systematically moved among female families in different generations was calculated. The change in heterozygosity showed a cyclical pattern of rises and falls, repeating in cycles of n-1 generations. The average rate of inbreeding per generation and the average inbreeding effective population size were approximately $1/[4N-(\log_2 N + 1)]$ and $2N-2$ respectively.

The realized rate of inbreeding and effective population size were studied in eight control populations of mice of different origins each maintained in two environments. The main populations were kept under controlled environmental conditions with 25 single pair matings, and one replicate was sampled from each population about generation 18 and was kept in an environmentally uncontrolled laboratory with 15 single pair matings. Cyclical mating system was followed in all the populations, and the realized inbreeding coefficient showed a repeating pattern of rises and falls over generations. Unequal contribution of different families to the subsequent generation resulted in the variance of family size to be larger than zero, and the realized effective population sizes were 33.7% to 65.5% smaller than the expected based on the planned breeding program. The genetically heterogeneous

populations had smaller variance of family size, larger effective population size and slower rate of inbreeding in both environments compared with those which had a longer history of inbreeding.

The frequency distributions of the first parity litters (N=22422) in different populations were examined. The distributions were all negatively skewed (P<0.01), indicating an excess of small size litters compared with normal distribution. The populations that were maintained in the controlled environment had greater skewness and showed larger deviations from normality than their replicates maintained in an uncontrolled environment. The mean litter size in several replicate populations were significantly larger than those in the main populations.

There were significant differences in litter size between generations in almost all the populations. A fairly good agreement existed between the expected genetic heterogeneity of the populations and their within generation mean-squares. The trends of litter size by generations were highly variable in different populations, and the negative trends were not likely due to inbreeding depression alone, as the pooled linear regression coefficients of litter size on percent inbreeding were insignificant in most of the populations. Time series analysis showed that there were patterns in the fluctuation of mean litter size from generation to generation in most of the populations, but the patterns were not consistent across the populations. The results suggested that neither the fluctuations nor the trends of mean litter size over generations could be fully attributable to the environmental variations, and the genetic constitution of the populations should have also influenced the patterns of variations and the trends.

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I. GENERAL INTRODUCTION

Application of quantitative genetic theories and advanced management techniques have resulted in considerable improvement in productivity of farm animals during the past few decades. The genetic theories were established mostly by R.A. Fisher, J.B.S. Haldane and S. Wright around 1920. The subject was expanded by geneticists and statisticians, mainly based on the foundation laid down by these three scientists who used the concepts of the Mendelian genetics. Today there is a substantial body of theory and large amounts of experimental data which substantiate the theory in considerable detail, showing that genes contributing to variation of any quantitative trait do have the properties known from Mendelian genetics, when extended to the properties of populations and to the simultaneous segregation of genes at many loci. Extension of the Mendelian inheritance principles to populations resulted in understanding numerous genetic phenomena such as pleiotropy, linkage, mutation, chance, variable expression, and the effects of non-genetic factors on the expression of quantitative traits.

The available theories of quantitative genetics allow us to predict the consequence of any specific breeding plan, and to compare the merits of alternative procedures for animal and plant experiments. However, a vast array of factors may play a role in determining the results of any breeding plan. Chance, and many other difficult-to-measure factors are potent forces which may alter the results drastically. In dealing with breeding problems, search for methods which reduce the chance of error is of considerable importance. Solutions to the problems in livestock breeding may partly come from results of experiments with laboratory animals and plants, from the experiments with particular species of livestock or by use of computer programs which attempt to simulate procedures thought to be applicable to livestock breeding, serving as guidelines for setting up animal breeding plans or to aid in interpretation of results of the experiments. These sources could all contribute to the better understanding and more precise application of the available theories in quantitative genetics.

Laboratory organisms have contributed greatly to present knowledge of quantitative genetics, and have a long history as materials for genetic research which goes back to the 19th century. After rediscovery of Mendel's findings in 1900, numerous experiments with laboratory organisms were initiated to investigate hereditary problems, and the results were interpreted in the light of Mendel's discoveries. W.E. Castle working with *Drosophila* (Castle *et al.*, 1906), Sewall Wright with guinea pigs (Wright, 1922) and H.D. King with rats (King, 1911, 1918a,b,c) were among the pioneers. The common house mouse (*Mus musculus*), an easy to handle mammal with relatively short generation interval, became a very suitable material for many different types of genetic research. Today, a vast literature is available in which the mouse has been used as the experimental animal in studies of different quantitative genetic problems. The relevance of genetic experiments with mice to problems in animal breeding have been discussed by Chapman (1961), Roberts (1965) and McCarthy (1982) in review papers. The general conclusion is that the mouse cannot be considered as an excellent analogue for farm animals, and the results of the experiments involving the mouse do not have direct application in farm animal breeding. Nevertheless, the results of experiments with the mouse have been very helpful in understanding the genetic control of quantitative traits, and could be regarded as an indication of possible outcome in animal breeding programs. Even with the rapid advancement of biotechnology and mammalian recombination genetics, the mouse is still a valuable mammalian model in genetic research (Wagner *et al.*, 1981a,b).

The main objectives of experiments with laboratory organisms are (Falconer, 1981):

i-Quantitative genetic theory has far outstripped both experimental and application aspects of livestock and plant breeding, and laboratory organisms allow examinationof the validity of the theories.

ii-Experimental study of laboratory organism populations allows deduction of the properties of genes associated with quantitative variation. Validity of conclusions from experiments concerning gene actions depend on repeatability of the experimental results.

iii-There may be new phenomena which cannot be predicted from the theory, and careful studying of the experimental results may lead to discovery of such new phenomena.

These three points were the underlying objectives and the general guidelines for all the analyses conducted in the present work.

Information about the history of the mice used, methods of formation of the populations and management practices are presented in detail in chapter II. Obviously, without a clear understanding of the materials used and the managerial practices followed, the analyses would be biased and interpretation of the results would be inaccurate. It was not, however, easy to gather the necessary information, due to the time interval and complexity of the project. It should be acknowledged that, despite many difficulties which existed on the way in carrying out this project, a very large volume of data has been recorded in its best possible form with a surprisingly high degree of accuracy.

Chapter III deals with the theoretical aspects of a cyclical mating system which was followed in this experiment although very little information was available about it. What is presented in this chapter is the result of hundreds of pages of mathematical calculations and a large volume of computer work condensed into a few formulae. This chapter which comprises a small portion of this work reflects more than 60% of the time devoted to the entire thesis. The theoretical findings about cyclical mating system were compared with the real data in Chapter IV. The main thrust of Chapter IV was on the study of the effects of the expected genetic heterogeneity of the populations and environment on breeding structure of the populations, namely effective population size and variance of family size.

Several factors influence the genetic constitution of a population and phenotypic value of a trait. Simultaneous consideration of all these forces requires huge facilities and considerable man-power to conduct an experiment, and mathematical models which would be too complicated to handle. One way to overcome such difficulties is to remove all but one or two sources of variation. In a control population, all the factors which change the genetic structure of a population with the exception of inbreeding, genetic drift and mutations are being held constant. The various analyses which were performed in the last two chapters aimed at explaining the patterns of variation of litter size over many generations in such a relatively simple situation. In other words, the primary objective was not to prove or disprove any predetermined theory, rather to search for phenomena, and trying to explain the findings on the basis of available knowledge on the genetic control of litter size.

The data set is unique in a sense that there has been no attempt so far to keep more than two large control populations for so many generations in laboratory mammals.

The relatively large number of populations of different origin, each maintained in two environments, large number of successive generations connected by known pedigree, and the large number of families per generation provided an excellent opportunity for a comprehensive study of any trait. Yet, the size and the structure of the data made it difficult to condense the information into a form that could be easily comprehended without losing much of its significance. Furthermore, the available information was a by-product of programs designed for other purposes, rather than the result of a specifically designed experiment (the data set used in the present work is a small part of a large selection experiment). There are obviously many limitations inherent in the structure of the data which would limit more elaborate analytical work and interpretation of the results. The data set included the records of 217,982 individual mice, and due to its large size, many of the ordinary methods of checking and rearranging the data were not easily applicable in this case. Several FORTRAN programs had to be written to make the data ready for any type of analysis. Working with such a large data set was a laborious, challenging and computationally costly task, yet the valuable experiences gained were certainly worth the input.

II. SOURCE OF DATA

II.1. Personnel

The available data belong to the Agriculture Canada Research Station at Lacombe, Alberta. The mice project was originally started by Dr. J.A. Newman and Dr. H.T. Fredeen in 1961. The mice laboratory was under the supervision of Jim Bar from the beginning until the summer of 1968, followed by Ev Gilmar who was responsible from 1968 to 1973 when Dawn Sumner assumed the responsibility.

II.2. History of mice used

Inbred lines:

Two pairs of mice, each pair consisting of one brother and one sister, from each of the four highly inbred strains; A/J, RFM, DBA/1 and C57-BR/cd; were obtained from the Jackson Memorial Laboratories, Bar Harbour, Maine, in August 1961. DBA was one of the first inbred lines of mice established. Its history goes back to 1909 when C.C. Little, who was studying the inheritance of coat color in mice under W.E. Castle, obtained a pair of mice carrying the recessive genes for dilution, brown, and non-agouti. During the next few years Little mated the descendants of his pair of mice brother to sister or parent to offspring for more than 20 generations, accompanied with selection for vigor. Twice during that period the line of descent had been narrowed to a single pair. He named this line "dbr" which was later called "dba" after the three recessive genes in the line. Since about 1950 it has been written "DBA" (Murray, 1934; Staats, 1966).

In 1913, H.T. Bagg obtained some albino mice from a dealer in Ohio (U.S.A.), maintained them as a closed colony and used them in behavioural experiments. In 1921, L.C. Strong mated a mouse of the Bagg's albino stock with one from an albino stock maintained by Little at the time at Cold Spring Harbor. From this cross Strong started the "A" strain (Strong, 1936), which had high incidence of mammary and lung tumors (Heston, 1949). The line was divided into several different sublines, among them A/J with low incidence of mammary tumor (Jackson Memorial Laboratory, 1955).

In 1921, C.C. Little obtained some mice from a fancier in Massachusetts and mated two black littermates. Brother to sister mating of the progeny of this pair, which segregated as black and brown, resulted in two strains, one of which was called C57BR (Heston, 1949; Staats, 1966). The history of the inbred RF strain (also called RFM) goes back to 1928 at the Henry Phipps Institute in Philadelphia (Furth *et al.*, 1933).

The inbred lines used in this experiment were the sublines of the above mentioned lines which have been kept by the Jackson Memorial Laboratory since around 1948 (Jackson Memorial Laboratory, 1955). These inbred mice have mainly been raised for medical research purposes, with a long history of inbreeding before arrival at the Jackson Memorial Laboratory. Small or medium-size colonies of the inbred lines of mice, which are called "inbred nucleus" are maintained at the Jackson Memorial Laboratory. Each line was maintained by single pair matings. Relatively large colonies (usually 140 matings each) have been maintained as "supply stocks". These colonies were cut back to the offspring of single pairs within two generations. The offspring from these colonies are supplied as identified brother-sister pairs to the breeding sections, from which offspring were available to those who requested them. Jackson Memorial Laboratory guarantees that their mice are never more than five generations removed from a narrow inbred line whose characteristics are constantly being studied and recorded (Jackson Memorial Laboratory, 1955).

Non-inbred strains:

Four non-inbred strains of mice; Q, NB, JH and XL were imported from the Institute of Animal Genetics, Edinburgh, Scotland. The JH-strain was the high-litter size selection line of Dr. Falconer's experiment. The base population, which was designated as J, had been a heterogenous line of mixed origin. It had been made from crosses between Bateman's high-lactation line, Goodale's and MacArthur's large body weight selected lines, and four mutant stocks with the C57-BL inbred lines as parts of their ancestry

(Bowman and Falconer, 1960). They stated that this population "was about as close as one could get with laboratory mice to a natural random-bred population". The details of the selection procedure and the response to selection have been reported by Falconer (1955, 1960b, 1963, 1971). Briefly, the line had been kept by 10 pairs of mice per generation, with the avoidance of sib and first cousin matings. Response to selection had ceased after about 20 generations of selection with the mean litter size of about 9.2, compared to 7.6 in the control. The inbreeding coefficient of the strain was about 32% in generation 31, a few generations before it was shipped to Lacombe.

The Q strain was established with the objective of achieving a broad spectrum of genetic variation, and it had a substantially heterogeneous background (Garnett and Falconer, 1975). One half of the ancestry of the Q-strain was from a cross between the JU inbred line and a control line (JC) both derived from the J-stock, as was explained above. Another half was from crosses between McArthur's and Goodale's large body weight selected strain, McArthur's small body weight strain, Falconer's high litter size selected strain (JH), and a sample of the J-stock, selected for high growth rate on a restricted diet (Falconer, 1960a). The detail of all lines of ancestry of the Q-strain have been traced back to around 1948 and presented by Falconer (1973). After its formation by Bruce Cattanach, the Q-strain was maintained by minimal inbreeding for nine generations with 10 pair matings per generation. Dr. Falconer took over this strain in 1960, thereafter it was maintained with minimal inbreeding with 20 males and 40 females per generation.

The NB strain belonged to Dr. Nigel Bateman (ABRO, Roslin, Edinburgh). This was a non-inbred strain which had been formed originally from crosses between non-selected strains. The XL was made by crossing four strains plateaued for large body-size.

Ten pairs of mice from each of the JH and Q strains and 15 pairs from each of the XL and NB strains were imported to Lacombe in September 1961.

II.3. Formation of the stock populations

All the inbred lines, A/J, C57BR/cd, DBA/1 and RFM, which will be referred to as A, C, D and R respectively, were propagated as inbreds during late 1961. In February 1962, all 12 possible reciprocal crosses were made among the four inbred lines, using 3 males and 3 females from each of the lines. These mice were kept long enough to raise up to six litters. In May 1962, 20 pairs of the crossbred progeny from the early parities were crossed again so that all resultant progeny had ACRD genotype, as shown below (male X female):

CR X AD, 1 mating, AD X CR, 2 matings
RD X AC, 2 matings, AC X RD, 1 mating
CD X RA, 1 mating, RA X CD, 1 mating

DC X RA, 2 matings, RA X DC, 2 matings
DR X CA, 3 matings, CA X DR, 3 matings
DA X CR, 1 mating
DR X AC, 1 mating

Progeny of these matings were called generation zero of population IC (300/1).

The progeny of the 2-way crosses from the later parities were mated in September 1962 and six crossbred groups were generated as follows (male X female):

i-Five RC X RC matings were made to produce the first generation of the RC line. No CR crossbred was available for mating. This line died out after four generations due to infertility of the parents or death of the progeny.

ii-Generation one of RA line was made by five pairs of RA X RA matings. No AR mouse was available. This line became extinct after 3 generations.

iii-DA line was established by mating 10 pairs of DA mice. No AD mice was available for mating. This line became extinct after 5 generations.

iv-DR line was established by three DR X RD and five RD X RD matings. This line died out after two generations.

v-Ten AC X AC matings were made to produce generation one of the AC line. No CA crossbred was available for mating. This line survived and was called population AC (301/1).

vi-Three CD X CD, three DC X DC, two CD X DC and two DC X CD matings produced generation one of the CD line which survived and was called population CD (302/1).

All the mice imported from Edinburgh were mated as straightbreds in late September 1961, soon after arrival at the Lacombe Experimental Station. The XL, Q, NB and JH-strains were named population LXCL (400/1), QL (500/1), NBL (600/1) and JHL (700/1) respectively. The populations LXCL and NBL will be referred to as LX and NB respectively. The JHL showed some infertility and young mortality, and could not be continued more than 3 generations. Its extinction could have been, at least partly, due to inbreeding, which was at least 32% at arrival. The mice in all the populations during the first three generations were kept to raise up to 6 litters. Some of the progeny from the later parities of generation one and early parities of generation two of each of the four populations (also a few original mice from the JH strain) were crossed in March 1962, as shown below:

i-Ten JH X Q matings produced JQ crossbred group.
ii-Ten NB X Q matings produced NQ crossbred group.
iii-Fourteen NB X XL matings produced NL crossbred group.
iv-Twelve JH X XL matings produced JL crossbred group.

The crossbred progeny were again mated in late May 1962 so that the next generation had equal proportion of genes from each of the four strains. The mating design was as follows:

NL X JQ, 20 matings
JQ X NL, 10 matings
JL X NQ, 15 matings

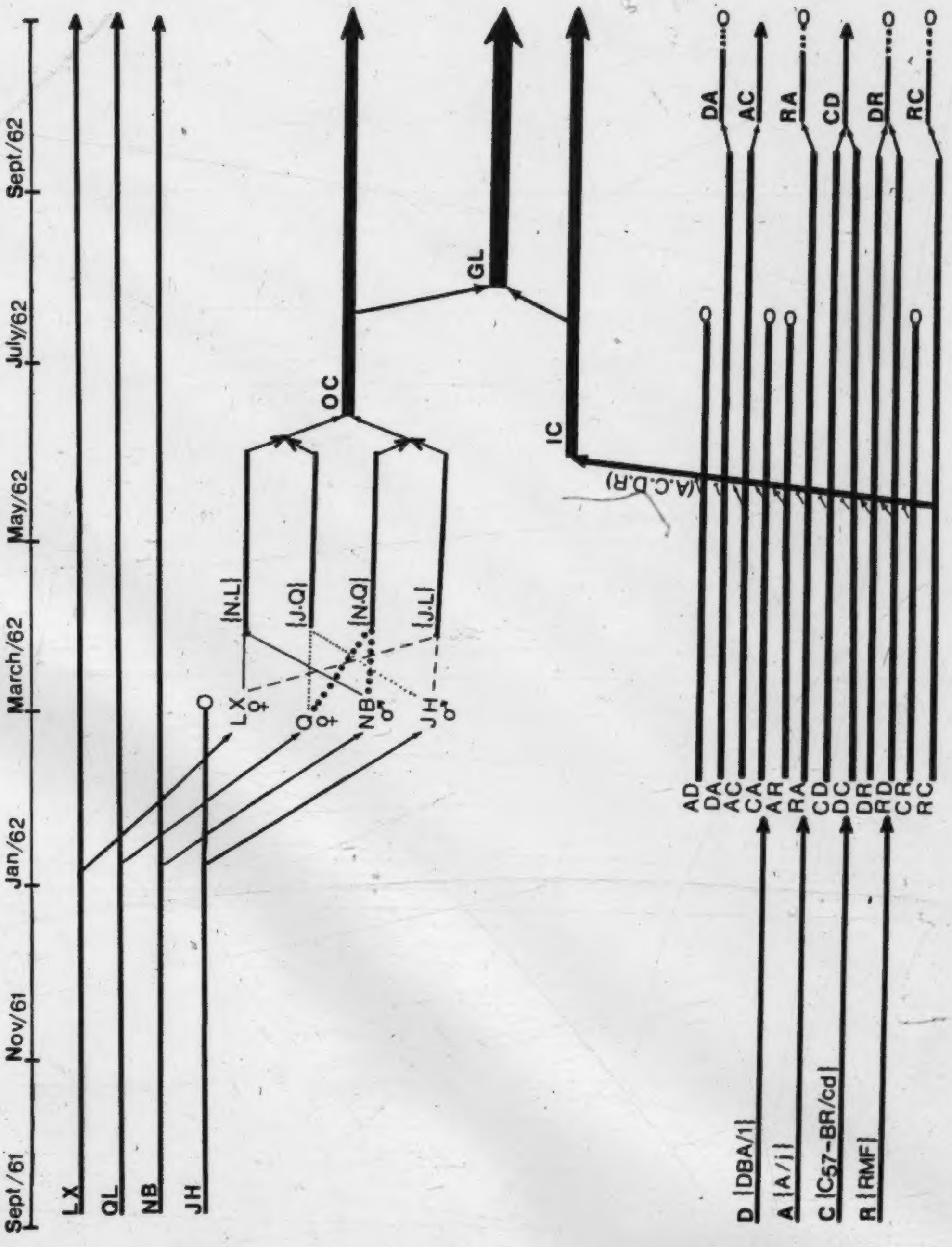
Sept/61
Nov/61
Jan/62
March/62
May/62
July/62
Sept/62
LX
QL
NB
JH
LX ♀
Q ♀
NB ♂
JH ♂
(N.L)
(J.Q)
(N.Q)
(J.L)
OC
GL
IC
(A.C.D.R)
D (DBA/1)
A (A/J)
C (C57-BR/cd)
R (RMF)
AD
DA
AC
CA
AR
RA
CD
DC
DR
RD
CR
RC
DA
AC
RA
CD
DR
RC

Figure II.1 Mating design used to generate the stock populations. The circles indicate termination of the lines.

NQ X JL, 15 matings

The progeny of these matings were designated as generation zero of population OC (200/1). Stock population GL (100/1) was formed in August 1962 by reciprocal crossing of 100 males and 100 females from each of the populations OC and IC. Mating patterns used to form the stock populations are graphically shown in Figure II.1, and information about them are summarized in Table II.1.

One replication from each of the 8 stock populations which survived was sampled between 1964 to 1966 by taking 15 pairs of mice from each population. Not more than two mice were selected from each family in so far as possible. The only exception was the replicate of the population NB which started with five pairs of mice, but four of them did not produce any live progeny, and the parents of the first generation were all full-sibs (4 males and 5 females). The replicates will be designated by adding the letter "R" to the name of the main population. Some information about the replicates are shown in Table II.2.

II.4. Genetic heterogeneity of the foundation stocks

Information about the genetic heterogeneity of the foundation stocks would be helpful for the interpretation of the results. History of the mice and the method by which the stocks were formed provide some information, although very crude, about their genetic heterogeneity. A hypothetical random-bred population of laboratory mice could be

Table II.1

Some information about the stock populations

Population identification	Pairing date first generation	Number of generations studied	Method of generating population
QL (500/1)	1961/272†	72	non-inbred
LX (400/1)	1961/272	73	non-inbred
NB (600/1)	1961/272	73	non-inbred
OC (200/1)	1962/240	69	QL * LX * NB * JH
AC (301/1)	1962/260	69	A * C57-BR
CD (302/1)	1962/260	69	C57-BR * DBA
IC (300/1)	1962/240	69	A*C57-BR*DBA*RFM
GL (100/1)	1962/323	67	IC * OC

†Day one is January first.

considered as a reference point to which all the populations will be compared. Generation one of the populations AC and CD were genetically equivalent to progeny of a single individual selected from a random-bred population and propagated by self-fertilization, and consequently were 50% inbred. These populations are expected to have a very narrow genetic background. Generation one of the population IC was equivalent to progeny of mating between a family of full-sibs whose parents were selected from a random-bred population, and therefore were 25% inbred. The population OC was possibly the most heterogeneous of all the populations, because it was constructed by crossing four non-inbred populations. More detailed information on the genetic diversity of the populations are presented in Appendix II.1.

Table II.2

Some information about the replicates of the stock populations

Replicate identification	Pairing date of the first generation	Generation of the stock population sampled
QL-R (501/1)	1964/328†	13
LX-R (400/2)	1966/354	22
NB-R (600/2)	1966/018	17
OC-R (201/1)	1964/328	9
AC-R (301/2)	1966/258	17
CD-R (302/2)	1966/096	15
IC-R (300/2)	1966/257	17
GL-R (100/2)	1966/362	17

†Day one is January first.

II.5. Management

The mice were kept in two laboratories, one was environmentally controlled at 22±1° C temperature and 45±5 % relative humidity (A-lab). The other laboratory was a poorly heated, poorly air conditioned building (C-lab). Maximum temperature in the C-lab, which fluctuated with outside temperature, was around 30° C, and minimum was mostly above freezing point, but occasionally reached the freezing point. A thermo-humidigraph recorded the temperature and humidity. The laboratories were light sealed and a controlled 12-hour light cycle was provided with a small light left on during the dark period. All the stock populations were kept in the A-lab while their replicates were maintained in the C-lab since the first generation.

Wire top, 8 X 10 inch aluminum cages with deep-drawn feeders were used to keep the mice. Coarse pine sawdust was used as bedding and pine shavings was also provided as nesting material, when necessary. All cages were cleaned once per week. The mice were fed a pelleted mouse breeder ration *ad libitum* . This diet was composed of ground whole wheat, casein, dried skim milk, dehulled 50% soybean meal, fish meal, corn oil, brewers yeast, stabilized Vitamin A and D, salt and ferric citrate. It was guaranteed by the manufacturer[1] to contain a minimum of 19% protein, 11% fat, and 52% nitrogen free extract and a maximum of 2.5% crude fiber. The ration was not changed throughout the course of the experiment.

Matings, with a few exceptions, especially during the early generations, were made every 91 days, resulting in four generations per year. The mice were between 7 and 10 weeks (mainly 8 and 9 weeks) of age when bred for the first time. Only the first parity litters were used for breeding in so far as possible. Males and females were together for 17 days after pairing. The females were checked for pregnancy 17 days after pairing and the pregnant females were caged separately. They were subsequently examined daily for littering. The mice were mated within a few days in each generation. During the first few generations and when a population had fertility problems, the mice were kept to raise more than one litter.

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[1] Ration 911R, manufactured by the Emory Morse Co., Box 313, Guildford, Conn., U.S.A.

II.6. Mating Plan

All the stock populations, except the population GL, were maintained with 25 single pair matings per generation which were used in a special mating plan. Stock population GL was maintained with a breeding sample of 49 males each mated to two females until generation 24 and with 50 males each mated to 2 females in each generation thereafter. The replicates of the stock populations were all raised with 15 single pair matings per generation. The number of pair matings deviated from those figures, especially during the early generations, because it was necessary to propagate enough mice to expand the stock populations, to create crossbred populations, and to provide mice for other experiments. When the signs of low fertility and/or high young mortality were shown by a population, attempts were made to increase the number of matings above those numbers in order to save the population; yet, occasionally the number of matings declined due to fertility problems.

One male and one female were selected from each litter as the parents for the next generation. The foundation pairs were given a family number from one to n (n was 25 in the main population, 50 in the GL and 15 in the replicates). The son was given the family number of his sire, while his mate came from another family varying systematically in different generations. Males of the r-th family in generation 1, 2, .

. t' within each cycle (t'=n-1) mated with females belonged to families r+1, r+2, . . r+t' to produce generations 2, 3, . . t'+1=1, respectively. Each cycle took n-1 generations. This mating system will be referred to as *cyclical mating*, and will be discussed in detail in the next chapter.

It was not possible to follow this mating pattern in all the generations, mainly due to failure of a litter to provide the required healthy progeny, sire and/or dam infertility or death. Unhealthy and abnormal individuals were not selected for breeding. If none of the progeny was vigorous and his/her life expectancy was in doubt, a litter-mate of the same sex was also held as a spare, so that if the first died before mating the second would still be alive for replacement. When there was no young available for selection in a family, substitutes for male, female or both were obtained from other litters, mainly from those which gave birth earlier with some degree of attention to the number of healthy progeny weaned in the family. Selection of breeding individuals within each litter was not strictly random, but was rather toward average 42-day weight. The very heavy and/or very light individuals of each dam family,if any, were discarded and a table of random numbers was used to choose breeders among the rest of the young. The selection and the mating plan used in this experiment had the following implications:

i-It maximized effective population size and thus minimized rate of inbreeding.

ii-Between family environmental effects (such as maternal effect) were removed, and consequently the possibility of selection for maternal effects were minimized.

iii-Method of selecting the individuals within each family greatly reduced selection differential for all the traits, particularly 42-day weight.

II.7. Measurements

Each female had a litter card on which sire and dam identification number, pairing date, population number, generation number, litter number, ear notch number, coat color of sire and dam and date of birth were recorded. Number and sex of live and dead born young, and total weight of live young were recorded on the first day of birth. In some cases it was not possible to identify the sex of a new born young with certainty, and the young was categorized as unidentified. Weaning was at 21 days of age and sex, individual weight (to the nearest 0.1 g), and tail length (in millimeter) were recorded. Individual body weight and tail length were recorded again at 42 days of age. In addition, color and disposal date of the young along with disposal reason were recorded. Body weight and tail length were not measured in any of the replicates which were kept in the C-lab, nor in the main populations for a period of a few years, due to lack of personnel.

III. INBREEDING UNDER CYCLICAL MATING SYSTEM

III.1. Abstract

General recursion formulae for the coefficient of inbreeding under a cyclical mating system were derived in which one male and one female are selected from each of the n families per generation (population size N=2n). Each male is given the family number of his sire in each generation, while his mate comes from another family, varying systematically in different generations. Males of the r-th family in generations 1, 2, 3, . . t'=n-1 within each cycle mate with females from families r+1, r+2, r+3, . . r+t' to produce generations 2, 3, 4, . . t'+1=1, respectively. The change in heterozygosity shows a cyclical pattern of rises and falls, repeating in cycles of n-1 generations. The rate of inbreeding oscillates between <-3% to >6% in different generations within each cycle, irrespective of the population size. The average rate of inbreeding per generation is approximately $1/[4N-(\mathrm{Log}_2\ N + 1)]$, which is the rate for the maximum avoidance of inbreeding (Wright, 1965). The average inbreeding effective population size is approximately 2N-2.[2]

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[2] A version of this chapter was reviewed by Dr. Alan Robertson of the University of Edinburgh and Dr. C.C. Cockerham of the North Carolina State University, and accepted for publication in Theoretical and Applied Genetics.

III.2. Introduction

Need for a quantitative measure of degree of inbreeding was realized in early 1900's. Pearl in a series of papers (1913, 1914c, 1915, 1917a,b) tried to quantify the degree of inbreeding and relationship in the form of a *coefficient*, which was later modified by Ellinger (1920). The coefficient of relationship proposed by Pearl (1914c) furnished a rough index of the probability that the two germ plasms which unite to form an individual are alike in their constitutions. Wright (1921, 1922b) used path analysis approach and defined the coefficient of inbreeding (f) as the correlation between uniting gametes. Several others attacked the problem of inbreeding using probability arguments (Haldane and Moshinsky, 1939; Cotterman, 1941; Malecot, 1948). Malecot (1948) defined the probability that the homologous genes of two individuals are identical by descent, i.e. of being copies of the same ancestral gene. Different terminology has been used in the literature to define the probability that any two genes at a particular locus have the same origin, and the term *coefficient of identity* will be used in this text. While Malecot's definition of the coefficient of identity would lead to the same result as does Wright's path coefficient method (Wright, 1965), the former is easier to grasp, and requires simpler probability arguments.

Progress in understanding the concept of inbreeding and the way it influences the phenotype of an individual has come through linking inbreeding with Mendels' laws, i.e., the effect of inbreeding on homozygosity. Even before the turn of the century, it was known that the direct effect of continued inbreeding is reduction in heterozygosity. As a matter of fact, Mendel (1865) in computing the F_3 families expected from selfing F_2 plants, showed how self-fertilization would affect the zygotic composition of a population. Mendel, in his original paper (1865), indicated that if equal fertility of all plants in all generations is assumed, and if every plant always self-fertilized, then in the n-th generation, the ratio of any particular allelomorphic pair (A, a) would be 2^n-1 (AA) : 2 (Aa) : 2^n-1 (aa) .

The first attempt to mathematically analyze the effect of some regular systems of mating on heterozygosity was that of Pearl (1913), who mistakenly concluded that inbreeding does not change heterozygosity. He later corrected his mistake (1914a), and several other papers were published on the same subject within a few years (Fish, 1914; Pearl, 1914b, 1915). The approach of these researchers was to write out all the possible matings generation after generation and calculate the rate of decline in heterozygosity. Jennings (1914, 1916) and Robbins (1917) expressed homozygosity at various generations of several regular mating systems in terms of mathematical series. Their formulae not only simplified calculation of homozygosity at any generation, but also helped to figure out the limiting values of homozygosity when regular systems of mating continue for many generations. Wright(1921, 1931, 1965) presented formulae that would express the average consequence of inbreeding in any kind of mating system in which the relationship between the mates could be formulated definitely. He extended his idea to include the inbreeding which occurs merely because populations are finite in size, and showed its identity with the random drift in gene frequency.

Bartlett and Haldane (1934) used matrix algebra to study inbreeding with sib mating at a tetrasomic locus. They showed that the asymptotic rate of progress toward homozygosity is the largest non-unit latent root (eigenvalue, λ) of the generation (transition probability) matrix. This method was used to find homozygosity in cases with two loci (Haldane, 1937), and when the frequencies of different alleles were not the same (Haldane, 1955). Fisher (1949) used matrix algebra to compute the increase in homozygosity of sib mating in diploids and tetraploids, first-cousin mating, and other simple systems. The method of using generation matrix gives a more complete account of the consequences of systems of mating, and is very simple to handle with computers. Under regular mating systems, it is possible to write the heterozygosity of individuals in any two generations in the form of $H_t = G\ H_{t-1}$, where H_t is the vector of heterozygosity of the individuals in generation t, and G is generation matrix. It could be easily shown that:

$$H_t=G\ H_{t-1}=G\ (G\ H_{t-2})=G^2H_{t-2}=G^tH_0$$

Where H_0 is the original heterozygosity of the population. The relationship between inbreeding coefficient (F), which measures the level of homozygosis in a particular population relative to some standard, and λ, which is the rate of change in homozygosity at the state of steady decay, is $F_t=1-\lambda^t$, where t is the number of generations of inbreeding.

In farm animal breeding, particularly in control populations, the aim is to use mating systems which will retain the original genetic constitution with as little change as possible, i.e. to minimize rate of inbreeding and genetic drift. The mating systems which minimize one effect do not necessarily minimize the other (Kimura and Crow, 1963 a,b). There is a vast literature on the theoretical rate of inbreeding and genetic drift variance under various mating systems, many of them summarized by Wright (1969) and Crow and Kimura (1970). Consider a population of bisexual organisms with constant size over generations. It is now well known that when the number of males and females are equal and each breeding parent is represented by exactly one offspring of each sex in the next generation, both the inbreeding and drift effective numbers will increase approximately twofold, compared with a case in which the number of progeny is random (Wright, 1938, 1965; Crow, 1954; Gowe *et al.*, 1959b; Latter, 1959; Kimura and Crow, 1963b;

Robinson and Bray, 1965). However, since the increment in gene frequency drift is proportional to the heterozygosity in the previous generation, any mating system which minimizes the amount of heterozygosity also minimizes the gene frequency drift (Kimura and Crow, 1963a). This implies that the population should be split into many lines and inbreeding should be practiced within the lines so that the mates become more related than the average relationship within the population as a whole (Robertson, 1964). Such a strategy is not practical in maintaining control populations of farm animals because inbreeding depression cannot be easily overcome without high selection pressure (Hill, 1972a). Consequently, those systems which minimize the rate of inbreeding have been more extensively utilized in farm animal breeding. Further reduction in the rate of inbreeding, over what can be achieved by equalizing the number of progeny per parent, can be reached by imposing the restriction of avoiding mating between closely related individuals (Wright 1921, 1951, 1965; Robinson and Bray, 1965; Cockerham, 1970).

Before the publication of the Kimura and Crow (1963a) paper, it was generally accepted that maximum avoidance systems of mating (Wright, 1921) had the slowest rate of inbreeding. They (Kimura and Crow, 1963a) found that although the maximum avoidance system had the slowest initial rate of decrease of heterozygosity, there were other systems, which they called "circular mating" and "circular pair mating", that had more remaining heterozygosity in later generations. They showed that in circular mating, in which each individual was mated with the one to his right and to his left, and circular pair mating, in which each male (or female) progeny moved one cage to the right, lead to asymptotic rates of decrease in heterozygosity of $1-\lambda=\pi^2/(2N+4)^2$ and $1-\lambda=\pi^2/(N+12)^2$ respectively. Although circular mating is extremely effective in slowing down final rate of homozygosity, it is not a convenient system in practice because each individual has to be mated twice. Furthermore, decrease of heterozygosity is always more rapid in the circular and circular pair matings than the maximum avoidance systems during the earlier generations, after which the latter starts to lose heterozygosity more rapidly. It is after about 65 generations in a population of size 16 and after about 160 generations in a population of size 32 that rate of decrease in heterozygosity under circular pair mating falls below that of maximum avoidance (Kimura and Crow, 1963a).

The cyclical mating systems are easy to follow at the practical level, and have been in use for some time; for example, in the mouse colonies of Agriculture Canada Research Station at Lacombe, Alberta (since 1961), and the University of Melbourne, Australia (Beilharz, 1972, 1982), and in some swine populations in Australia (Beilharz, presonal communication). One type of cyclical mating system with the objective of minimizing the rate of inbreeding in purebred livestock populations was briefly discussed by de Rochambeau and Chevalet (1982). One of the advantages of these systems over maximum avoidance systems (Wright, 1921, 1965) is that the former can easily be used with any number of breeding pairs, while the latter is convenient to use only when size of breeding population is an integral power of 2 (N=2, 4, 8, 16, etc.). Little published material is, however, available on these systems. Cockerham (1970) briefly discussed cyclical matings as a class of mating systems which do not form permanent sublining. Beilharz (1982) has used a cyclical mating system in which one of the pairs (female) of generations 1, 2, 3, 4, . . t moved to families n+1, n+2, n+4, n+8, . . $n+2^{t-1}$ to produce generations 2, 3, 4, 5, ... t+1. Beilharz (1982) computed the inbreeding coefficient of the first 25 generations in a population of size 40 by the method of coancestry, and found the pattern of rises and falls in the inbreeding coefficient.

The objective of this study was to compute the theoretical rate of inbreeding and inbreeding effective population size under a cyclical mating system, and compare that with other mating systems aiming at minimizing the rate of inbreeding. It is assumed that the generations do not overlap, and each family leaves only two progeny per generation, and therefore, the population size remains constant.

III.3. Cyclical mating system

Suppose one male and one female are selected from each of the n families per generation (population size N=2n). The foundation pairs are given a family number from 1 to n. One of the mates, say male, is given the family number of his sire in each generation, while his mate comes from another family, varying systematically in different generations. Males of the r-th family in generations 1, 2, 3, . . t' within each cycle (t'=n-1) mates with females from families r+1, r+2, r+3, . . r+t' to produce generations 2, 3, 4, . . t'+1=1, respectively. The cycle is repeated after each n-1 generations. Figure III.1 shows the cyclical mating system for a population with six pairs. This system is, of course, one of many possible types of cyclical matings (Cockerham 1970).

III.4. Recurrence equations

When two individuals A and B are related, they may carry identical copies of genes received from their common ancestors at any randomly selected locus, i.e., the genes are *identical by descent* (Malecot, 1948). The *coefficient of identity* of individuals A and B, $\Phi(A,B)$, is defined as the probability that a gene taken at random from A is identical by descent with a gene at the same locus taken at random from B. The coefficient of identity of an individual by itself, $\Phi(A,A)$, is the probability that two genes randomly selected, one after the other, from the same locus in

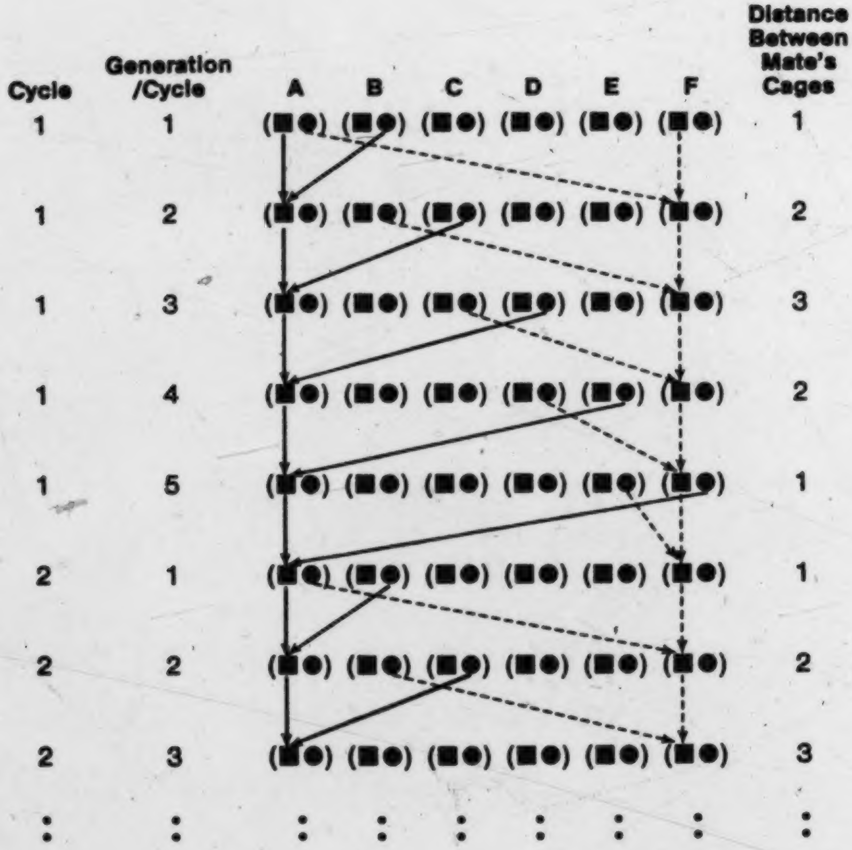
Cycle
Generation /Cycle
A
B
C
D
E
F
Distance Between Mate's Cages
1
2
3
4
5

Figure III.1 Cyclical mating system in a population of size 12. Only the parents of individuals born in cages A and F are shown.

individual A, are identical by descent. The coefficient of inbreeding of individual A (f(A)) is the probability that the two genes at a randomly selected locus in individual A are identical by descent. Considering a neutral autosomal gene in a dioecious organism in which Mendelian segregation occurs, the basic equations defining the genetic relationship between individuals are:

$$f(A)=\Phi(F_1,M_1) \tag{1}$$

$$\Phi(A,A)=(1/2)\ [1+\Phi(F_1,M_1)]=\ (1/2)[1+f(A)] \tag{2}$$

$$\Phi(\text{Full-sibs})=(1/4)[2\Phi(F_1,M_1)+\Phi(F_1,F_1)+\Phi(M_1,M_1)]=$$
$$(1/2)\{(1/2)[\ f_{(t-1)}\ +1]+\Phi(F_1,M_1)\} \tag{3}$$

$$\Phi(A,B)=(1/4)[\Phi(F_1,F_2)+\Phi(F_1,M_2)+\Phi(M_1,M_2)+\Phi(M_1,F_2)] \tag{4}$$

Where F_1, F_2, M_1 and M_2 are fathers and mothers of individuals A and B respectively (Jacquard, 1974). For the unrelated individuals, or those in the original generation whose genealogical relationships are not known, it is assumed that $\Phi(A,B)=0$, and $\Phi(A,A)=1/2$.

The recurrence equations 1 to 4 connecting homozygosity (f) and coefficients of identity (Φ) in successive generations were applied to populations of various sizes subjected to continued cyclical mating system. The results showed that the equations for f and Φ's are not the same in all generations, but two cyclic patterns were detected. Firstly, the set of equations are repeated after a cycle length of j=n-1 generations, i.e., equations for generations 1 to n-1, n to 2n-2, 2n-1 to 3n-3, etc., are the same. Secondly, there is a symmetry for the recurrence equations within each cycle. Considering the cages as points on a circle, and "k" as the shortest distance between any two points, then the maximum number of steps between any two cages is m=n/2 if n is even and m=(n-1)/2 if n is odd. The coefficients of identity between any two individuals "k" steps (cages) apart, either to the right or to the left, are the same in each generation. The equations for generations 1, 2, 3, . . m within each cycle are the same as those for generations n-1, n-2, n-3, . . m, respectively. The homozygosity of an individual for any one of the possible alleles at a locus at generation t is:

$$f_t(A)= \Phi_{t-1}(i) \qquad (5)$$

$$i=t' \text{ if } 1\le t'\le m$$

$$i=n-t' \text{ if } m<t'\le n-1$$

Where t' and i stand for generation within each cycle ($t'=1+[(t-1) \bmod n-1]$), and type of equation respectively. In this case, type of equation "i" in each generation is the same as the number of steps "k" between cages. The general formula for the probability that the homologous genes taken one from each of the two individuals born in the same cage (zero step apart, k=0) in generation t be identical by descent is:

$$\Phi_t(0)=(1/2)\{(1/2)[1+f_{t-1}]+\Phi_{t-1}(i)\} \qquad (6)$$

$$i=t' \text{ if } 1\le t'\le m$$

$$i=n-t' \text{ if } m<t'\le n-1$$

Let $\Phi_t(k)$ be the probability that any two randomly chosen homologous genes in two individuals k ($1\le k\le m$) cages apart are identical by descent in generation t. Then the recurrence equations for individuals 1, 2, . . k cages apart are:

$$\Phi_t(1)=(1/4)[\Phi_{t-1}(i-1)+2\Phi_{t-1}(1)+\Phi_{t-1}(i+1)] \quad (7)$$

$$\Phi_t(2)=(1/4)[\Phi_{t-1}(|i-2|)+2\Phi_{t-1}(2)+\Phi_{t-1}(i+2)] \quad (8)$$

. . . .

$$\Phi_t(k)=(1/4)[\Phi_{t-1}(|i-k|)+2\Phi_{t-1}(k)+\Phi_{t-1}(p)] \quad (9)$$

$i=t'$ if $1\le t'\le m$ $\qquad$ $i=n-t'$ if $m<t'\le n-1$

$p=i+k$ if $i<m-k+1$ $\qquad$ $p=n-i-k$ if $i\ge m-k+1$

t'=Generation within cycle$=1+[(t-1) \bmod n-1]$

The method of derivation of the equations are presented in Appendix III.1 in more detail.

It is more convenient to use heterozygosity ($H_t=1-f_t$) and coefficient of non-identity ($\Psi_t(k)=1-\Phi_t(k)$). Equations 5, 6 and 9 then take the following forms:

$$H_t=\Psi_{t-1}(i) \quad (10)$$

$$\Psi_t(0)= (1/4)H_{t-1}(i)+ (1/2)\Psi_{t-1}(i) \quad (11)$$

$$\Psi_t(k)= (1/4)[\Psi_{t-1}(|i-k|)+ 2\Psi_{t-1}(k)+ \Psi_{t-1}(p)] \quad (12)$$

III.5. Generation matrices

The recurrence equations (10,11,12) can be easily presented in matrix form. There are j=n-1 generation (transition probability) matrices within each cycle which are of m different types. Examples of the generation matrices are presented in Appendix III.2. There are some

Table III.1

Rate of decrease of heterozygosity per cycle (1-Hc), average rate of inbreeding per generation (ΔF), and average effective population size (Ne) under cyclical mating system in populations of size 8 to 52

N†	j‡	(1-Hc)	ΔF	Ne
8	3	.104080	.035971	13.90
10	4	.106905	.027870	17.94
12	5	.109442	.022915	21.82
14	6	.110483	.019323	25.88
16	7	.112063	.016836	29.70
18	8	.112116	.014754	33.89
20	9	.113236	.013264	37.69
22	10	.113319	.011955	41.82
24	11	.113853	.010928	45.75
26	12	.113947	.010031	49.85
28	13	.114433	.009304	53.74
30	14	.114236	.008627	57.96
32	15	.114778	.008095	61.77
34	16	.115813	.007663	65.24
36	17	.115718	.007208	69.37
38	18	.115995	.006826	73.25
40	19	.115992	.006468	77.30
42	20	.116046	.006148	81.32
44	21	.116100	.005859	85.33
46	22	.116225	.005600	89.28
48	23	.116134	.005353	93.41
50	24	.116287	.005138	97.32
52	25	.116252	.004931	101.40

† Population size

‡ Number of generation per cycle.

differences between intracyclic patterns of matrices, depending on whether n is even or odd. The generation matrices for the odd values of n have the size s=(n+3)/2 and appear in the following pattern within each cycle:

$$\Omega = G_1\ G_2\ G_3\ .\ .\ G_{m-1}\ G_m\ G_m\ G_{m-1}\ .\ .\ G_3\ G_2\ G_1$$

The matrices for even n's have size s=(n+4)/2 and appear in the following form for each cycle.

$$\Omega = G_1\ G_2\ G_3\ .\ .\ G_{m-1}\ G_m\ G_{m-1}\ .\ .\ G_3\ G_2\ G_1$$

The first and the last matrix in each cycle (G_1) is the same as the generation matrix of the circular pair mating (Kimura and Crow 1963a). Many of the matrices for each population size can be transformed to each other using permutation matrices. In particular, if n is an odd prime, and one of its least positive or least negative primitive roots is even (Abramowitz and Stegun 1970), i.e. n=5,7,11,13,19, etc., then the permutation matrix (P) is primitive and its factorization consists of one cycle of full length m (Davis 1979). In such cases $P^m=I$, where m is the number of different types of matrices within the cycle, and all the matrices can be transformed to each other with the operation $G_z=P'G_xP$. The eigenvalues of the matrices which can be transformed to each other are the same. More information about the relationships between generation matrices are given in Appendix III.3.

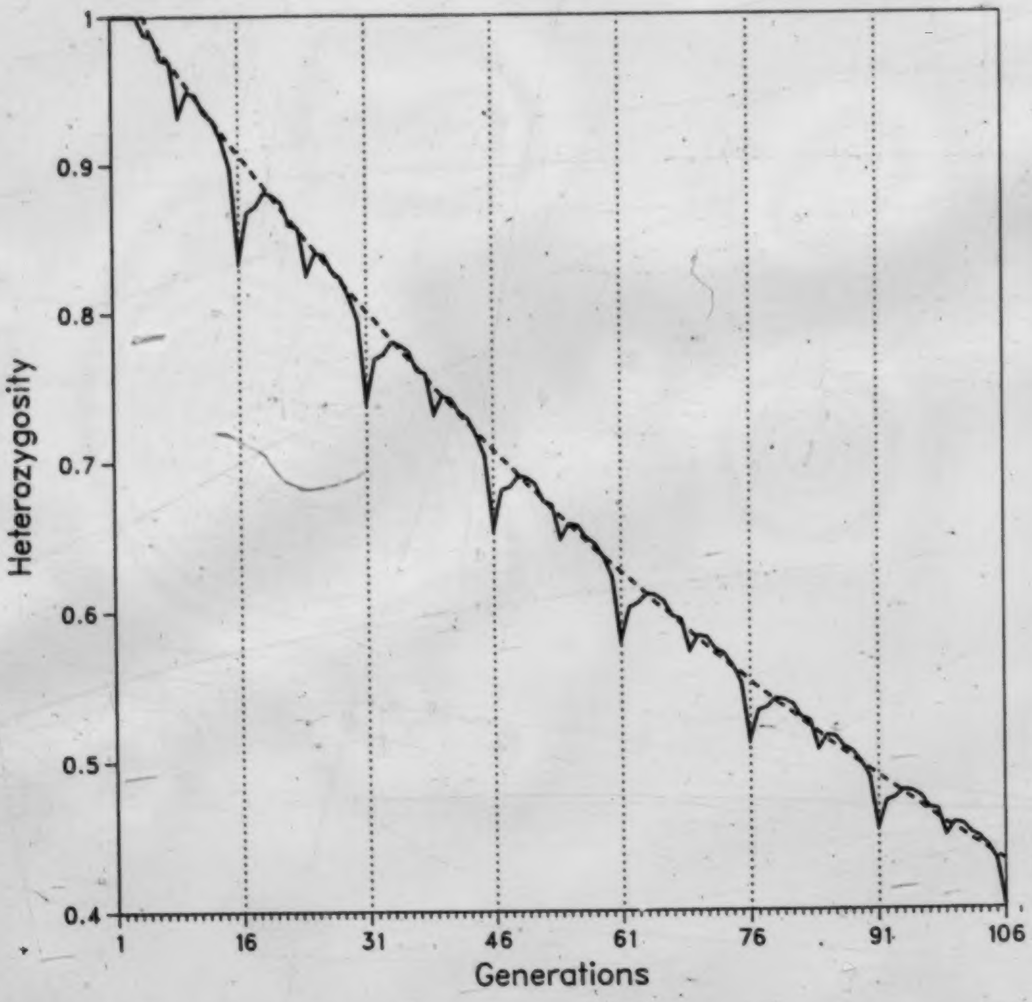

Figure III.2 Decrease in heterozygosity in a population of size 32 for the cyclical mating (solid line) and maximum avoidance of inbreeding (broken line)

III.6. Rate of inbreeding and effective population size

When a cyclical mating system has been continued for several generations (after the second cycle for $N>16$), the proportional change in heterozygosity per cycle (Hc) becomes equal to a constant value for each population size.

$$Hc=(H_{t+j}/ H_t)=\lambda$$

Where *j* is the cycle length and λ is the largest eigenvalue of Ω (the generation matrices for one cycle). The values for the rate of change of heterozygosity per cycle (1-Hc) are presented in Table III.1

The decrease in heterozygosity (H_t/H_0) with a continued cyclical mating system shows a repeating pattern of rises and falls from generation to generation, which is in contrast to all other regular mating systems that have been reported so far. The amount of heterozygosity in successive generations in a population of size $N=32$ is shown in Figure III.2. A corresponding plot for the maximum avoidance (Wright, 1921) in a population of the same size is also presented for comparison. The cyclical mating system precludes inbreeding for the first four generations when population size is larger than 18.

Under the cyclical mating system, the rate of change of inbreeding in each generation of the second cycle is exactly similar to the corresponding generations in all the succeeding cycles. There is large variation in ΔF from generation to generation within each cycle for the cyclical mating, as shown in Tables III.2 and III.3. The intracyclic

Table III.2

Rate of change of inbreeding per generation (X100) in populations of size 8 to 36.

Generation within cycle	Population size														
	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36
1	7.170	7.767	6.442	7.669	6.733	7.217	6.774	6.931	6.939	6.878	6.962	6.887	6.926	6.897	6.908
2	-1.879	-2.462	-3.216	-3.580	-3.595	-3.557	-3.749	-3.747	-3.774	-3.852	-3.876	-3.848	-3.880	-3.870	-3.883
3	5.268	7.767	2.871	0.946	0.335	0.144	-.030	-.126	-.240	-.266	-.321	-.350	-.388	-.409	-.415
4		-2.462	2.806	7.240	1.424	1.575	0.135	-.486	-.720	-.849	-.957	-1.021	-1.076	-1.118	-1.148
5			2.312	-3.071	4.129	6.355	2.336	2.170	2.623	0.994	0.930	0.483	0.271	0.171	0.101
6				1.789	-.859	-3.725	2.974	6.227	-.018	1.580	1.048	1.953	0.530	0.279	0.305
7					3.261	1.939	-1.116	-3.544	3.550	6.232	0.986	-.084	1.680	1.483	1.941
8						1.288	2.106	-.378	-1.462	-3.848	3.393	6.513	0.292	0.422	-.443
9							2.154	2.449	2.173	-.509	-1.635	-3.902	3.565	6.536	0.814
10								1.874	0.302	1.552	0.475	-.772	-1.662	-3.968	3.563
11									2.230	1.391	1.702	2.210	0.181	-.805	-1.730
12										2.131	1.043	-.063	1.288	0.360	0.079
13											1.941	1.297	0.578	1.972	1.770
14												2.125	1.429	-.022	-.226
15													1.990	1.529	0.912
16														2.026	1.064
17															2.108

Table III.3

Rate of change of inbreeding per generation (X100) in populations of size 38 to 52.

Generation within cycle	Population size							
	38	40	42	44	46	48	50	52
1	6.877	6.918	6.884	6.897	6.893	6.898	6.894	6.888
2	-3.902	-3.905	-3.911	-3.906	-3.914	-3.917	-3.919	-3.921
3	-.433	-.443	-.451	-.462	-.469	-.473	-.479	-.482
4	-1.175	-1.196	-1.210	-1.226	-1.239	-1.248	-1.258	-1.265
5	0.045	0.006	-.025	-.053	-.074	-.091	-.107	-.120
6	-.156	-.218	-.361	-.440	-.488	-.523	-.552	-.575
7	0.926	0.687	.605	.689	.263	.162	.139	.002
8	1.335	1.191	1.875	.299	.596	.495	.316	.529
9	-.007	0.258	-.429	1.415	1.153	1.899	.520	.230
10	6.643	0.849	.348	-.237	.165	-.574	1.395	1.156
11	-3.895	3.472	6.704	.944	.389	.207	-.316	.157
12	-.955	-1.786	-3.960	3.547	6.667	.939	.539	.131
13	0.232	-.006	-.933	-1.793	-3.974	3.549	6.657	.980
14	1.522	0.267	.056	-.071	-.983	-1.786	-3.985	3.519
15	0.385	1.536	2.161	-.036	.012	-.117	-.998	-1.817
16	0.683	-.039	-.482	1.410	.537	-.146	-.049	-.136
17	1.236	0.854	.381	.263	1.546	1.982	.431	-.212
18	2.142	1.339	.930	.682	-.286	-.392	1.195	.436
19		1.982	1.188	.488	.675	.114	.233	1.548
20			2.115	1.270	.692	.775	.153	-.339
21				2.091	1.305	.639	.786	.639
22					2.064	1.319	.626	.431
23						2.045	1.234	.632
24							2.084	1.296
25								2.082

pattern is, however, constant from cycle to cycle. The rate of inbreeding is more than 6.4% in the first generation of each cycle regardless of the population size. In populations where the number of families (n) is odd, a large positive value of ΔF (>6%) also occurs in the (j+2)/2 th generation within each cycle. When n is even, the second largest positive value of inbreeding rate occurs in the (j+3)/2 th generation within each cycle. The large positive value of ΔF is followed by a large negative value, indicating that some of the heterozygosity which was lost in the previous generation is immediately recovered. The sharp fluctuation in the rate of inbreeding is important when inbreeding depression is being studied. Beilharz (1982) reported that the overall reproductive performance of a population of mice under a cyclical mating system dropped in those generations in which inbreeding rose sharply.

The average rate of change in inbreeding per generation ($\Delta\overline{F}$), i.e., the constant rate of change which would have resulted in the same amount of inbreeding over the period of j generations, was computed from the relationship:

$$Hc = (1-\Delta\overline{F})^{j} = \prod_{i=1}^{j} (1-\Delta F_{i})$$

where, j is the number of generations in each cycle and ΔF_i (i=1,2, . . j) is the rate of inbreeding per generation. When the stage of steady decay is reached, $\Delta\overline{F}$ will have a constant value. The average rate of inbreeding per generation and the average inbreeding effective population size ($\overline{N}e=1/2\Delta\overline{F}$) for populations of size 8 to 52 are

Table III.4

The average rate of inbreeding per generation computed by different methods† in a population of size 18, and percent deviation of the computed from the asymptotic value

Cycle	Generation number‡	Method 1 ΔF	Method 1 %dev.¶	Method 2 ΔF	Method 2 % dev.	Method 3 ΔF	Method 3 %dev.
6	41	.015447	4.70	.015148	2.67	.014780	.17
6	42	.014233	-5.53	.013880	-5.92	.014760	.04
6	43	.013930	-5.58	.013577	-7.98	.014701	-.36
6	44	.013973	-5.29	.013629	-7.63	.014662	-.63
6	45	.015128	2.54	.014790	.24	.014760	.04
6	46	.013994	-5.15	.013607	-7.77	.014711	-.29
6	47	.014111	-4.36	.013736	-6.90	.014681	-.49
6	48	.014085	-4.53	.013717	-7.03	.014652	-.69
7	49	.015332	3.91	.014961	1.40	.014770	.11
7	50	.014318	-2.95	.013908	-5.73	.014760	.04
7	51	.014062	-4.69	.013654	-7.46	.014721	-.22
7	52	.014096	-4.46	.013696	-7.17	.014681	-.49
7	53	.015071	2.15	.014673	-0.55	.014760	.04
7	54	.014109	-4.37	.013675	-7.31	.014721	-.22
7	55	.014207	-3.71	.013783	-6.58	.014701	-.36
7	56	.014182	-3.87	.013766	-6.70	.014681	-.49
8	57	.015249	3.36	.014828	0.50	.014770	.11
8	58	.014379	-2.54	.013928	-5.60	.014760	.04
8	59	.014158	-4.04	.013709	-7.08	.014730	-.16
8	60	.014185	-3.86	.013744	-6.85	.014701	-.36
8	61	.015029	1.86	.014588	-1.12	.014760	.04
8	62	.014193	-3.80	.013724	-6.98	.014730	-.16
8	63	.014277	-3.23	.013817	-6.35	.014711	-.29
8	64	.014255	-3.38	.013802	-6.45	.014701	-.36

†-Method 1: $(1-1/2\overline{Ne})^t=\Pi^t_{i=1}(1-1/2Ne_i)$ or $1-F_t=(1-\Delta\overline{F})^t$,
Method 2: $(1/\overline{Ne})=1/t\ \Sigma^t_{i=1}(1/Ne_i))$,
Method 3: Regression of $\log(1-F_t)$ on generation number

‡-The last generation included in the computation.

¶-Percent deviation of the computed from the asymptotic value of $\Delta F=.014754$.

presented in Table III.1. The average rate of inbreeding per generation and the average inbreeding effective population size are close to $1/[4N-((\log_2 N + 1)]$ and $2N-((\log_2 N + 1)/2)$ respectively, which are the values for the maximum avoidance of inbreeding for population size which is an integral power of 2 (Robertson 1964, Wright 1965). The average rate of inbreeding is the asymptotic value around which the actual rates oscillate. The inbreeding effective population size is approximately 2N-2.

When effective population size is not constant over generations, the harmonic mean $(1/\overline{N}e=1/t \sum_{i=1}^{t} (1/Ne_i))$ is often used as the approximate solution to the equation

$$(1-1/2\overline{N}e)^t=\prod_{i=1}^{t} (1-1/2Ne_i).$$

In the present case, however, it was found that the harmonic mean of effective population size over each cycle is larger than that obtained from the exact solution. This is in agreement with the findings of Karlin (1968) and Motro and Thomson (1982) who dealt with the population sizes that were changing cyclically.

In practice, when $\Delta\overline{F}$ is computed from the relationship

$$(1-1/2\overline{N}e)^t= \prod_{i=1}^{t} (1-1/2Ne_i),$$

which is equivalent to and gives the same results as the equation $1-F_t=(1-\Delta\overline{F})^t$, or equation

$$1/\overline{N}e=1/t \sum_{i=1}^{t} (1/Ne_i),$$

the value of $\Delta\overline{F}$ would be above or below the average asymptotic rate if the last generation of inbreeding is taken in those generations in which it is maximum or minimum within each cycle respectively. The method of regression of $\log(1-F_t)$ on generation number ($\Delta\bar{F}=1-\exp(b)$) gives estimates which are less fluctuating with the final value of F. The numerical values for the average rate of inbreeding per generation computed by the different methods, and the percentage deviations of the computed and the asymptotic values in the case of N=18 are presented in Table III.4. All methods are sensitive to the value of t; the larger the number of generations of inbreeding, the closer the estimate of average inbreeding to its asymptotic value. Nevertheless, the dependency of the rate of inbreeding on t computed from the regression method is far less than those computed from the other methods.

IV. REALIZED INBREEDING AND EFFECTIVE POPULATION SIZE

IV.1. Abstract

The realized rate of inbreeding and effective population size were studied in eight control populations of mice of different origins each maintained in two environments. The main populations were kept under controlled environmental conditions with 25 single pair matings, with the exception of one population (GL) which was maintained with 50 males each mated to two females. One replicate was sampled from each population about generation 18 and was kept in an environmentally uncontrolled laboratory with 15 single pair matings. One male and one female were selected for breeding from each family and were used in a cyclical mating system.

The realized inbreeding coefficient showed a repeating pattern of rises and falls over generations, which was due to the systematic movement of females among the male families. The realized effective population sizes were 33.7% to 65.5% smaller than the expected based on the planned breeding program in different populations, although the size of the breeding section of the populations were maintained at what they were originally planned in most of the generations. Unequal contribution of different families to the next generation, caused by infertility of the mates, unequal sex ratio and/or mortality of all the progeny,

resulted in the variance of family size being larger than zero in almost all the generations in all the populations. This study demonstrated that the demographic properties of each population depended largely on the history of inbreeding and genetic variability of the original population. It was concluded that the genetically heterogeneous populations had smaller variance of family size, larger effective population size and slower rate of inbreeding in both environments compared with those which had longer history of inbreeding, including two- and four-way crosses between inbred lines.

IV.2. Introduction

Natural populations have generally complex breeding structures, which are difficult to define mathematically. It is often assumed that matings in natural populations are random as that simplifies the mathematical description of genetic consequences of breeding in a finite population. The concept of effective population size (Ne) introduced by Wright (1931, 1938), is of great value in the mathematical treatment of various breeding structures. The concept of effective population size has been used in the literature largely from the theoretical side, and less attention has been paid to its estimate in real populations. Since effective population size, both in natural and laboratory populations, is a function of fitness traits, it is affected by genetic and environmental factors. Published work on breeding structure and effective population size of several large size contemporary populations of laboratory mammals maintained over a large number of generations are limited. The present data appear to be suitable for studying the effects of environment and genetic heterogeneity on the breeding structure of laboratory mice. The degree of agreement between the observed and expected effective population sizes in various populations used in this study will hopefully provide some information on the impact of some genetic and environmental factors on effective population size. The results of studies such as this, would be useful to better understand the breeding structure of natural populations. The effect of finite size of a population on its genetic structure can be viewed in three ways namely; inbreeding, random extinction, and variance effects (Crow, 1954). The effective population size of a particular population for these effects may not always be the same (Crow, 1954; Kimura and Crow, 1963b; Kimura and Ohta, 1971; Ewens, 1982). The inbreeding effective population size was the only effect considered in this study.

The genetic consequence of inbreeding is to reduce the probability of an individual being heterozygous at any given locus. The chance of homozygosity of genes at any loci which were initially heterozygous can be computed for any generation under any mating system, under the assumption of Mendelian inheritance. The change in homozygosity under different mating systems can be profoundly affected by selection, whether natural or artificial, which may act on a specific locus. In case heterozygotes are favoured, the rate of increase in homozygosity will be slowed down, or may even be prevented if selection force is sufficiently strong. Mutations and linkage also cause the realized level of homozygosity under any inbreeding system to be less than expected.

The absence of selection and mutation can hardly be considered valid assumptions, and consequently the inbreeding coefficient (F) does not accurately measure the probability of identity by descent (or loss of heterozygosity) at a large proportion of loci. Nevertheless, with the absence of any other measurement which could serve the purpose, F is a valuable parameter and is a useful measure of average reduction in heterozygosity for all loci over a defined period of time and with respect to a reference population. Furthermore, it has been shown that the change in homozygosity over a given number of generations calculated from the actual frequency of neutral genes is close to expectations based on F values (Falconer, 1981).

Calculation of inbreeding coefficient from pedigree, particularly in cases where the number of individuals per generation and the number of generations are large, is a cumbersome task. Formulae for estimating inbreeding coefficients of populations without using the pedigree, or when pedigrees are not known, would therefore be quite useful. There have been many attempts to estimate inbreeding coefficient in cases where the breeding structure of a population is known (number of breeding individuals, distribution of family size, contribution of each family to the next generation). Wright (1938) showed that the expected effective population size (Ne) in a random-bred population with M breeding males and F breeding females is Ne=4MF/(M+F). The underlying assumption of this formula is that each parent has an equal chance of contributing to the next generation but does not necessarily leave an equal number of offspring. The assumption of equal chance implies that the actual distribution of progeny number per parent follows a Poisson distribution. If population size is constant over generations, the assumption of Poisson distribution of family number implies that $\bar{k}=\sigma^2_k=2$, where $\bar{k}$ and σ^2_k are the mean and variance of the number of progeny per family contributing to the next generation. The differences in reproductive performance among parents would increase the variance of progeny size and decrease the effective population number. On the other hand, any deliberate balancing ~~of the number~~ of offspring per parent would decrease the variance of progeny number and increase the effective population size. Wright (1931) has shown that if the variance of family size is zero, i.e., each male and female leaves exactly one offspring per generation, the effective population size would be approximately twice the actual number of the breeding individuals, regardless of the system of mating used.

In populations of laboratory animals, even when the number of progeny per parent is planned to be constant, not all the families contribute equally to the next generation. Variations in fertility, mortality and sex ratio contribute to variation in the number of progeny per parent ($\sigma^2_k>0$). Wright (1938) provided the formula $Ne=(4N-2)/(\sigma^2_k+2)$ to estimate the effective population size for such cases. Kimura and Crow (1963b) extended the idea to the case of separate sexes and gave the relationship $Ne=(N'\bar{k}-2)/(\bar{k}-1+\sigma^2_k/\bar{k})$, where N' is the number of grandparents and k is the number of gametes contributed by them. With constant population size and equal number of progeny per parents this equation becomes $Ne=2N-2$.

The objectives of this study were to evaluate:

i-The effects of environment and the genetic heterogeneity of the populations on the realized effective population size, variance of family size and advancement in inbreeding.

ii-The accuracy of estimate of effective population size based on breeding structure of a population compared with that calculated from pedigree.

IV.3. Materials and Methods

The coefficient of inbreeding for all the individuals (N=217,982) was computed by the method of coancestry[3]. A

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[3] The inbreeding coefficients of four of the populations

FORTRAN program was written to calculate the coefficients of identity of individuals born in any two successive generations because mating was occasionally performed between some individuals in two successive generations. The data of the early generations of the main populations were added to the records of the replicates before the inbreeding of the latter was computed. The inbreeding coefficients of the base populations from Edinburgh were assumed to be zero, and those for the inbred lines were considered to be one. The inbreeding coefficients in the first generation of the OC and GL populations were not zero, as the pedigrees were traced back to generations -1 and -2 (original mice) respectively. Therefore, inbreeding coefficients for all the individuals were estimated with respect to the base populations.

The realized effective population size over the course of the study for each population ($\bar{Ne}$) was computed by three methods:

Method 1: $(1-1/2\bar{Ne})^t = \prod_{i=1}^{t} (1-1/2Ne_i)$, where t is the number of generations and Ne_i is the effective population size in each generation calculated from the relationships $Ne_i=1/2\Delta F_i$ and $\Delta F_i= (F_t-F_{t-1})/(1-F_{t-1})$. The above equation is mathematically equivalent to the relationship $F_t=1-(1-\Delta\bar{F})^t$, where F_t is the the inbreeding coefficient at generation t. In cases where inbreeding coefficient of the first generation was not zero, those two equations gave the same

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[1](cont'd) were computed at Lacombe by Dr. A.K.W. Tong.

result by adjusting F_t's for the initial values, i.e., utilizing the increments of inbreeding during the course of the study. The increment of inbreeding was computed as follows. Let $F_{t1.t0}$ and $F_{t2.t0}$ be the inbreeding coefficient at generations t_1 (the first generation) and t_2 (the last generation) with respect to the base population. The inbreeding coefficient at generation t_2 with respect to that in generation t_1 ($F_{t2.t1}$), i.e., the increment is:

$$(1-F_{t2.t1}) = (1-F_{t2.t0}) / (1-F_{t1.t0})$$

Method 2: Regression of log(1-F) on generation number. The effective population size was then computed as $\Delta\overline{F} = 1 - exp\ (b)$, and $\overline{N}e = 1/2\Delta\overline{F}$.

Method 3: The harmonic mean of effective population size per generation $[1/\overline{N}e = 1/t \sum_{i=1}^{t} (1/Ne_i)]$.

Although mating period, and therefore duration of parturition, was spread over a relatively short period of time, the size of the populations were continuously changing over the time span from birth to breeding due to mortality. As a result, the inbreeding coefficient of each population, defined as the average inbreeding coefficients of all the individuals at any particular time (Jacquard, 1974), was changing in each generation. The recording system of the present experiment allowed computation of the inbreeding coefficient of each population at birth, at 21- and 42-days of age and at mating. The effective population sizes of the populations over all generations computed from the realized rate of inbreeding at different stages were very similar.

The ratio of the realized effective population size, computed over all generations, at 21- and 42-days of age and at mating over that at birth were between unity to .91, despite rather large differences among the estimates in some generations. Therefore, all the calculations regarding the observed rate of inbreeding and effective population size were performed on the individuals selected for breeding at each generation.

The mean and variance of the progeny number selected for breeding from each family were computed for each generation, and their means were calculated over all generations for each population. The formula $Ne=(N'\bar{k}-2)/(\bar{k}-1+\sigma^{2}_{k}/\bar{k})$ (Kimura and Crow, 1963b) was used to compute the effective population size, and the results were compared with those computed from the pedigrees.

IV.4. Results

Inbreeding and effective population size:

The average inbreeding coefficients of each population showed a repeating pattern of rises and falls by generations, which was due to the systematic movement of females among the male families. The pattern was clear and regular in most of the populations, but it was irregular in some of the populations which frequently encountered severe fertility problems, leading to the disruption of the mating system in some generations. The inbreeding coefficients in the QL and QL-R populations, which were typical examples of the populations which did not have fertility problems are shown in Figure IV.1. In the QL population, as well as in some other main populations, the rate of increase in inbreeding coefficient was relatively rapid and did not show any cyclical pattern during the early generations because the populations were started with a relatively small number of mice and they had some fertility problems during the early generations. After a few generations, the pattern of rises and falls in cycles of 24 generations (N/2 -1) was observed in the main populations. Since there were sharp increases in inbreeding coefficient in the first and 12th generations of each cycle, the peaks appeared after each 12 generations. The cycle length in the replicate populations with 15 pairs is theoretically 14 generations, and peaks appeared at intervals of 7 generations in the observed inbreeding coefficients. In theory, the cyclical mating system should preclude inbreeding for the first four generations, but it was not observed in most of the populations in this study because of the small number of original mice and minor fertility problems during the early generations.

The inbreeding coefficients of the breeding individuals in generation one, in the last generation and the increment during the course of study are shown in Table IV.1. The estimates of realized effective population size by the three methods, using inbreeding coefficient of the breeding individuals, are presented in Table IV.2. The deviation of

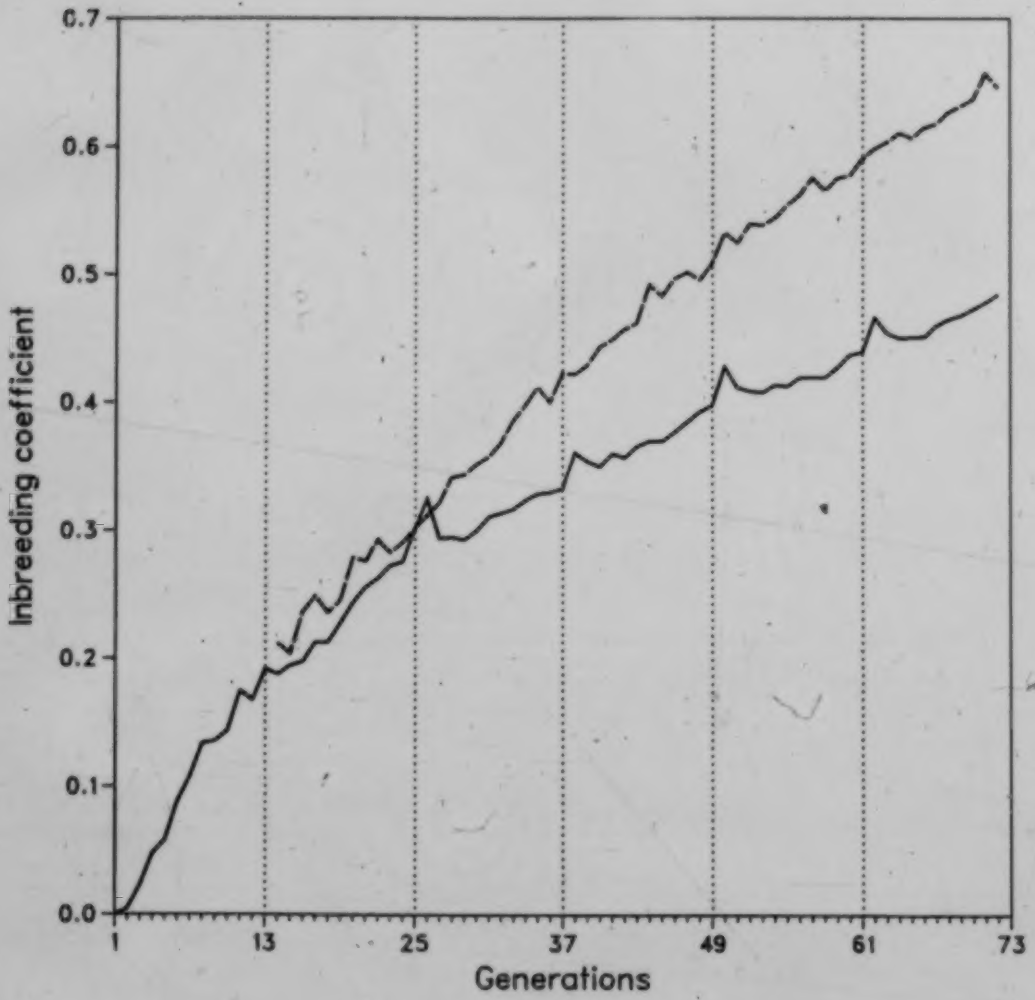

Figure IV.1 Inbreeding coefficient of the QL (solid line) and QL-R (dashed line) populations by generation

the realized effective population size computed by methods 2 and 3 as percentages of those estimated by the method 1 are also shown in Table IV.2. The estimates obtained from the harmonic mean method were consistently larger (between 0.9 to 3.2%) than those obtained by method 1 in all the populations. The deviation of $\overline{Ne}$'s estimated by methods 1 and 2 were very variable in different populations, ranging between +23.4% to -5.9%.

The realized rates of inbreeding in the populations were much faster than what were expected based on the planned population sizes and mating plan. The rapid rate of inbreeding was partly due to the fact that most of the populations were started with a small number of mice (10 or 15 pairs) and the population numbers were kept below 25 pairs during the early generations (the size of breeding segment of the replicates were 15 pairs from the first generation). Infertility and death losses contributed to deviations of the realized from the expected effective number after the size of the breeding segment of the populations were set at 25 pairs. Thus, effective population sizes in the main populations were computed starting from those generations in which the number of the breeding individuals were decided to be 25 pairs. The GL population was not included in this comparison because it was maintained by 49 males each mated to two females until generation 24, and 50 breeding males thereafter. The percentages of deviation of the realized effective

Table IV.1

Initial, final and the increment of inbreeding coefficients for sixteen populations

Pop.	Generation		Number of records	Inbreeding coefficient		
	Range	No.		Initial	Final	Increment
QL	1-72	71	18526	0.0	0.4850	0.4850
QL-R	14-72	58	7339	0.2123	0.6456	0.5501
LX	1-73	72	16532	0.0	0.5832	0.5832
LX-R	23-72	49	5643	0.3427	0.7762	0.6596
NB	1-73	72	14243	0.0	0.7022	0.7022
NB-R	17-71	54	6440	0.3343	0.8216	0.7321
OC	1-69	68	14873	0.0241	0.4407	0.4269
OC-R	10-68	58	8360	0.1195	0.5887	0.5328
AC	1-69	68	12779	0.5000	0.7533	0.5067
AC-R	18-68	50	5494	0.6075	0.8553	0.6313
CD	1-69	68	11497	0.5000	0.7894	0.5787
CD-R	16-68	52	6067	0.6476	0.8617	0.6076
IC	1-69	68	13631	0.2500	0.6014	0.4684
IC-R	18-59	41	4878	0.4076	0.7711	0.6136
GL	1-67	66	64262	0.0709	0.2229	0.1636
GL-R	18-67	49	7418	0.1289	0.5379	0.4695

population size from the expected values (the expected values are 97.3 and 57.9 for the main and replicate populations respectively, Table III.1) are presented in Table IV.3.

Effective population size in the main and replicate populations originated from crosses between non-inbred strains (GL-R, OC, OC-R) showed the least amount of deviation (<37.5%) from the expected. The QL and QL-R populations were also among those with relatively small deviations between the observed and expected effective population size. Effective population size in crosses between the inbred lines, and the LX population showed almost similar deviations from the expected within each environment. The realized effective population sizes were between 40.8% to 49.1% less than the expected in the main populations and between 52.2% to 62.2% in the replicates. The realized effective population size in the NB and NB-R populations showed the highest deviations from the expected (65.5%). The results also showed a fairly good agreement between the main and replicate populations in their ranking order for the deviation between the observed and expected effective population sizes within each environment.

Variance of family size:

The number of breeding individuals in a large portion of the generations in most of the populations was maintained as planned, but the number of individuals available for selection was below the desired number in some generations.

Table IV.2

Estimates of effective population size of the sixteen populations by three methods† and percent deviations from Method 1

Pop.	Method 1	Method 2	Method 3
QL	53.47	59.54 (11.3)‡	54.47 (1.9)
QL-R	36.56	35.14 (-3.9)	37.05 (1.3)
LX	41.38	47.96 (15.9)	41.75 (0.9)
LX-R	22.99	24.28 (5.6)	23.37 (1.6)
NB	29.97	29.34 (-2.1)	30.24 (0.9)
NB-R	20.75	25.61 (23.4)	21.41 (3.2)
OC	61.33	60.29 (1.7)	62.48 (1.9)
OC-R	38.35	39.77 (3.7)	39.09 (1.9)
AC	48.37	50.35 (4.1)	48.82 (0.9)
AC-R	25.31	23.80 (-5.9)	25.59 (1.1)
CD	39.58	47.60 (20.3)	40.22 (1.6)
CD-R	28.04	27.54 (-1.8)	28.48 (1.6)
IC	54.05	54.75 (1.2)	54.85 (1.5)
IC-R	21.81	21.08 (-3.3)	22.09 (1.3)
GL	184.96	198.98 (7.6)	187.24 (1.2)
GL-R	38.90	38.27 (-1.6)	39.57 (1.7)

†-Method 1: $(1-1/2\overline{Ne})^{t}=\Pi^{t}_{i=1}(1-1/2Ne_{i})$ or $F_{t}=1-(1-\Delta\overline{F})^{t}$.
Method 2: Regression of log(1-F) on generation number.
Method 3: Harmonic mean $(1/\overline{Ne})=1/t\ \Sigma^{t}_{i=1}(1/Ne_{i})$).

‡-Values in parentheses are percent deviations from the estimates obtained from Method 1.

Table IV.3

Percent deviations of realized effective population size from expected†

Population‡	% deviation	Population	% deviation
QL	-33.7	QL-R	-37.5
LX	-49.1	LX-R	-60.9
NB	-65.6	NB-R	-65.5
OC	-36.6	OC-R	-34.8
AC	-48.9	AC-R	-56.6
CD	-49.2	CD-R	-52.2
IC	-40.7	IC-R	-62.7
GL	.....	GL-R	-33.7

†-The expected effective population sizes were 97.3 and 57.9 for the main and replicate populations respectively.

‡-Realized effective population size was computed over those generations in which the intended number of breeding individuals was 25 pairs

Based on the number of families with live progeny at breeding, and the total number of individuals available for selection as breeders, the generations in which the number of breeding individuals were less than 25 and 15 pairs in the main and replicate populations respectively, were classified into the following two categories:

a-Generations having severe fertility problems. This group includes generations in which four or fewer families had live progeny, and thus the total number of individuals available for selection was much less than the predetermined number (generally less than 50%).

b-Generations having minor fertility problems. Generations in which a sufficient number of breeding individuals were not available, but five or more families had live progeny for selection were classified in this group.

In some of the generations in which a population showed severe fertility problems and the number of breeding individuals was small, the planned mating system was occasionally disrupted in order to save the populations from extinction. These disruptions in the planned mating system included harem mating (one male mated to more than one female), keeping mice long enough to produce litters in the second parity, and/or using some individuals from the parental generation for breeding (overlapping generations).

Table IV.4 shows the generation numbers in which the populations had fertility problems. The number of families with live progeny are also shown in parenthesis. The GL, GL-R, OC, OC-R, QL and QL-R populations did not have any fertility problem, and consequently, the predetermined population numbers were maintained in all generations. Populations which originated from crosses between inbred lines (AC, CD, IC) and the LX had fertility problems only in some of the early generations (generations one to 9), but the NB population showed frequent fertility problems over many generations. Replicates of the above populations encountered fertility problems in later generations. Problems in fertility and viability in the IC-R was so severe that the population could not be maintained and became extinct at generation 59. In addition, the NB-R population had severe fertility problems when it was sampled from the NB (generation 17). In that generation, only one out of the five pairs of mice selected from the main population was fertile, and this population started with a group of full brothers (N=4) and sisters (N=5).

Differences between the realized and expected effective population size were mainly due to unequal number of progeny per parents. Variance of family size measures the degree of differential contribution of different families to the next generation. The frequency distribution of the number of individuals selected for breeding per each family over all generations are presented in Table IV.5. The frequency of families which did not contribute any progeny to the next generation, due to infertility of parents or death of all the progeny, ranged between 14.8% (GL-R) to 35.1% (NB). The frequencies of these families were generally larger in the replicates than those in the corresponding main populations. The frequencies of families which contributed only one progeny to the next generation, due to presence of only one sex, were larger in the main populations than in the corresponding replicates in most cases. The frequency of the families from which two progeny were selected as breeders reflects the closeness of the actual selection of breeders and mating system to the original plan. The highest frequency of this class was 56% in the QL population, but in the LX-R and NB it was as low as 24%. The relative frequencies of different classes provide a basis for comparison among the populations for the combined effects of

Table IV.4

Generation numbers in which the populations encountered fertility problems

Pop.†	Generation number‡
LX	6(7), 7(5), 8(6), 9(9)
LX-R	55(2)*, 56(5), 60(4)*, 67(3)*, 68(3)*, 69(5)
NB	6(3)*, 8(6), 15(7), 16(5), 19(9), 20(9), 23(7), 31(8), 35(7), 38(8)
NB-R	17(1)*, 54(3), 55(4)*, 56(6), 66(5), 67(4)*
AC	2(7), 4(6)
AC-R	35(5), 48(3)*, 51(3)*, 52(4)*
CD	2(4)*, 3(4)*, 4(4)*, 5(6), 6(8)
CD-R	49(8), 55(7), 56(3)*, 57(5), 63(6)
IC	2(7)
IC-R	40(2)*, 47(8), 48(4)*, 51(2)*, 55(5), 56(2)*, 58(6), 59(4)*

†-Populations QL, QL-R, OC, OC-R, GL and GL-R did not have fertility problem.

‡-Generations identified by an asterisk are those which had severe fertility problem. Numbers in parentheses are the number of families which had live progeny.

fertility, litter size and viability on effective population size. Families from which a large number of progeny (more than 6) were selected were mostly those which were kept for more than one parity, either in those generations in which the size of the population had to be expanded (the first three generations in the main populations), or generations in which the populations faced severe fertility problems.

Table IV.5

Frequency distribution of the number of offspring selected for breeding per family by population

	Number of progeny selected per family										
Pop.	0	1	2	3	4	5	6	7	8	9	>9
QL	15.3	5.6	56.0	18.0	3.8	0.7	0.0	0.2	0.1	0.1	0.5
QL-R	18.1	3.6	45.3	26.6	5.7	0.7					
LX	28.5	3.9	32.0	24.3	7.9	1.1	0.7	0.5	0.3	0.4	0.7
LX-R	34.3	1.9	24.6	24.2	9.6	3.0	1.4	0.5	0.1	0.3	
NB	35.1	5.9	24.0	17.5	9.3	3.2	1.6	1.2	1.0	0.6	0.8
NB-R	31.0	4.6	24.2	25.9	9.2	2.4	1.6	0.4	0.4	0.4	
OC	16.7	4.2	50.0	22.5	6.2	0.2	0.0	0.2	0.1		
OC-R	15.1	2.6	55.0	22.4	4.3	0.6					
AC	25.7	3.5	31.8	27.3	9.5	1.2	0.4	0.1	0.1	0.1	0.2
AC-R	31.6	1.8	26.2	25.5	11.2	1.7	1.2	0.7	0.1		
CD	27.0	3.4	31.7	26.2	8.3	1.9	0.4	0.4	0.3	0.2	0.2
CD-R	27.0	4.8	32.4	23.5	8.4	2.1	1.1	0.1	0.4	0.0	0.1
IC	20.8	5.0	43.8	20.8	6.2	2.1	1.1	0.3			
IC-R	29.4	4.5	35.7	19.9	5.6	1.8	1.7	0.7	0.3	0.2	0.2
GL-R†	14.8	3.3	55.2	21.5	4.5	0.4	0.3				

† The population GL was not included because each male mated to two females.

The number of generations in which all the families contributed exactly two individuals to the next generation ($\sigma^2_k=0$) were indeed very small, ranging between zero to 5 in different populations (Table IV.6). The mean and standard deviation of the variance of family size for males, females and both sexes combined in each generation are presented in Table IV.6. The means of the variances of family size for both sexes combined per generation in more than half of the populations were more than 2, which is the variance of family size under random mating. The means of variances of family size in males, females and combined sexes in the main populations from Edinburgh and their crosses (QL, LX, NB, OC) were generally larger than those in their respective replicates, while the reverse situation was true for the AC and IC populations.

The ratio of effective population size computed from the formula $Ne_1 = (N'\bar{k}-2)/(\bar{k}-1+ \sigma^2_k/ \bar{k})$ over that computed from $Ne_2 = 2N-2$ would be unity if all families had equal contribution to the next generation ($\sigma^2_k=0$) and population size was constant ($\bar{k}=2$). The deviation of this ratio from unity measures the combined effects of unequal contribution of different families to the next generation and discrepancies in the original mating plan (overlapping generations, harem mating). The ratios exhibited in Table IV.7 show that the populations GL-R, OC, OC-R, QL and QL-R which did not have fertility problems ($\bar{k}$ was close to two in all the generations), the ratios of Ne_1/Ne_2 were the highest among all populations, ranging between 0.60 to 0.64. These values indicate that the variance of family size reduced the effective population size by about 40% in these populations. This ratio was smaller (between 0.53 to 0.09) in the other populations due to the combined effects of larger variance of family size (Table IV.6) and violation in the mating system.

Accuracy of estimating effective population without using pedigree:

The ratio of Ne_1 over the effective population size computed from the pedigree (Ne_3) indicates how accurately

Table IV.6

Number of generations in which variance of family size was zero, and mean and standard deviation of variance of family size per generation for males(M), females(F) and both sexes (M+F)

	Number of generations in which $\sigma^2_k=0$			Variance of family size					
				M		F		M+F	
Pop.	M	F	M+F	Mean	SD	Mean	SD	Mean	SD
QL	2	2	0	.537	1.293	.655	2.026	1.887	5.556
QL-R	3	2	2	.461	.283	.465	.253	1.406	.837
LX	0	0	0	.903	1.830	1.092	2.183	3.075	5.673
LX-R	1	1	1	.964	.871	.886	.623	2.928	2.108
NB	0	0	0	1.215	1.306	1.349	1.358	4.305	4.704
NB-R	1	1	1	.931	.878	1.095	1.232	3.067	2.964
OC	1	2	2	.452	.552	.427	.332	1.303	1.096
OC-R	6	5	5	.365	.258	.377	.282	1.286	1.154
AC	0	0	0	.695	.731	.732	.828	2.316	2.699
AC-R	2	2	2	.827	.606	.884	.637	2.734	2.021
CD	0	0	0	.789	.754	.872	1.044	2.670	2.891
CD-R	3	4	3	.756	.609	.797	.778	2.409	2.142
IC	3	2	1	.593	.571	.542	.528	1.771	1.883
IC-R	2	1	1	.926	1.168	.767	.726	2.682	3.114
GL†	8	3	2	.170	.348	.566	.603	1.012	1.330
GL‡	0	0	0	.298	.166	.335	.289	.853	.659
GL-R	8	4	4	.373	.333	.367	.330	1.179	1.164

†- Computed from the male families

‡- Computed from the female families

effective population size, and therefore rate of inbreeding, could be computed without using pedigrees. The estimates (Table IV.7) indicated that this ratio was larger than 0.9 in many of the populations, even in some populations such as CD in which occasionally the original mating system was disrupted. Therefore, the agreement between the estimates obtained from the formula or pedigree was fairly good even when the number of generations was fairly large. Frequent violation of the underlying assumptions upon which the formula was developed, resulted in weaker agreement, as expected.

IV.5. Discussion

Although cyclical mating is one of the systems of avoidance of inbreeding which have been known for a rather long time (Wright, 1921), the published articles mentioning the cyclical pattern of fluctuation in the inbreeding coefficient are limited to those of Beilharz (1972, 1982). He (Beilharz, 1982) computed the inbreeding coefficient of the first 25 generations of a population of size 40 by the method of coancestry, and found the pattern of rises and falls in the inbreeding coefficient interesting enough to report the phenomenon. He observed that the overall reproductive performance of a population of mice under a cyclical mating system dropped in those generations in which inbreeding rose sharply.

Table IV.7

Effective population size computed from the formula $Ne_1=(N'\overline{k}-2)/(\overline{k}-1+\sigma^2_k/\overline{k})$, and its ratios over $Ne_2=2N-2$ and that computed from the pedigree (Ne_3)

Pop.	Ne_1	Ne_1/Ne_2	Ne_1/Ne_3	Pop.	Ne_1	Ne_1/Ne_2	Ne_1/Ne_3
QL	55.48	.63	1.04	QL-R	33.96	.60	.93
LX	34.85	.38	.84	LX-R	11.38	.22	.50
NB	26.36	.30	.88	NB-R	15.08	.30	.73
OC	58.18	.61	.95	OC-R	36.33	.64	.95
AC	43.99	.50	.91	AC-R	19.04	.35	.75
CD	36.89	.43	.93	CD-R	26.42	.47	.94
IC	50.39	.53	.93	IC-R	4.07	.09	.19
GL	----	---	---	GL-R	36.43	.64	.94

Average realized effective population size is equivalent to a constant population number which would have resulted in the same rate of inbreeding over the same number of generations, and provides a tool for comparing different populations for the effect of population size on the rate of inbreeding. If population sizes were constant and the populations had either random, or a regular non-cyclical mating system (such as the maximum avoidance of inbreeding), then the three methods for estimation of the rate of inbreeding would have resulted in approximately the same values. The observed differences are due to the cyclical changes in the rate of inbreeding caused by the mating system, and due to the sharp jumps in the inbreeding coefficient in some generations when the populations encountered severe fertility problems. The estimates calculated by the methods 1 and 3 depend on the last generation in which the experiment stopped. If the last generation was one in which the inbreeding coefficient was maximum or minimum within each cycle, the computed effective population size would have been considerably different from that estimated using the inbreeding coefficient one generation back or one generation ahead. In cases where the effective population size is not constant over generations, the harmonic mean $[1/\overline{Ne}=1/t \sum_{i=1}^{t} (1/Ne_i)]$ is often used as the approximate solution to the equation $(1-1/2\overline{Ne})^t=\prod_{i=1}^{t} (1-1/2Ne_i)$. The results show that the harmonic mean of effective population size per generation is between 0.9% to 3.2% larger than the effective population size computed from the exact solution. The large differences between the two estimates (Table IV.2) were observed both in the populations which did not have fertility problems (QL, OC, OC-R) and those which had severe fertility problems (NB-R). The reason for the differences in the former group was fluctuations in the effective population size due to the mating system, and in the latter was due to variation in effective population size caused by both mating system and variations in the number of breeding individuals. The result is in agreement with the findings of Karlin (1968) and Motro and Thomson (1982) who dealt with population numbers which were changing cyclically. It can be shown that $1-[1/t \sum_{i=1}^{t} (1/N_i)] \geq [\prod_{i=1}^{t} (1-1/N_i)]^{1/t}$. Both sides of this equation are the same when all the N_i's are the same, and the difference becomes large as the variation between N_i's becomes larger.

Theoretically, the method of regressing $\log(1-F_t)$ on generation number seems to be preferable to the other two methods for comparative purposes in cases where inbreeding coefficients change cyclically (see chapter III), because the dependency of $\overline{Ne}$, estimated from the regression method, on the inbreeding coefficient in the last generation, is less than that for the other methods. Nevertheless, when there are sharp but non-cyclical increases in the inbreeding coefficient in some generations, or when the regression of $\log(1-F)$ on generation number is not linear, the method of regression would under- or over-estimate the realized rate of inbreeding. Since in none of the populations studied, the inbreeding coefficient of the last generation was minimum or maximum within a cycle, the values calculated from the formula $(1-1/2\overline{Ne})^t=\prod_{i=1}^{t}(1-1/2Ne_i)$ were considered to be the most accurate.

The main thrust of this section was on the comparison between the populations with different genetic heterogeneity for effective population size, rate of inbreeding and variance of family number. The deviation of realized effective population size from expected values based on the mating system (Table IV.3), the deviation of the variance of family size from zero (Table IV.6), and the ratio of Ne_1/Ne_2 (Table IV.7) reflect the combined effects of the overall reproductive potential and survival ability of the populations on the realized effective population size and increase in inbreeding coefficient. The genetic structure of the populations plays a major role on their ability to maintain their effective population number close to the census number of breeding individuals. The larger the genetic heterogeneity, or the shorter the inbreeding history of a population, the smaller the variance of family size, the lower the chance of deterioration of reproductive fitness due to environmental factors and/or inbreeding depression, and the closer the realized and expected effective population sizes. Rates of inbreeding and variance of family size were generally smaller and the effective population size was larger in the OC, OC-R GL-R, QL and QL-R populations compared with the other populations of comparable size. The OC and GL populations were of crossbred origin, and therefore were genetically heterogeneous (see Appendix II.1). Populations QL and QL-R performed similarly to the above two populations with respect to all the parameters studied, possibly because QL originated from crosses between several non-inbred strains (Falconer, 1973), with the objective of achieving a broad spectrum of genetic variation and substantial heterogeneous background (Garnett and Falconer, 1975). This study demonstrated that the populations with greater genetic diversity had slower rates of inbreeding under any particular breeding plan and census number at any environment as compared with the populations with longer history of inbreeding including the crosses between inbred lines. This conclusion is based on the fact that the populations ranked fairly similarly for all the parameters studied in both environments.

In this section, there will be no attempt to explain the reasons for the differential fitness of different populations, as this would require detailed analyses of all the components of fitness (fertility, litter size, survival ability). What can be concluded at this stage is that environmental factors were not the major reason, as the populations were contemporaneous within each environment and shared similar conditions. Deterioration of reproductive fitness due to inbreeding depression was expected to be the least in the crosses between inbred lines because such populations are supposed to be free of any lethal or semi-lethal genes, which are partly responsible for inbreeding depression. In litter bearing species, such as mice, particularly when population size is large, natural selection should be able to successfully reduce the frequency of lethal mutants without having an appreciable effect on the fitness value of a population. The fact that four out of six two-way crosses between inbred lines became extinct before the 6th generation demonstrates the importance of the level of genetic heterogeneity on the fitness value of a population.

The very few generations in which the variance of family size was zero indicate that unequal contribution of every family to the next generation is a rule rather than an exception. Attempts were made in this experiment to keep the variance of family size equal to zero, but in almost all the generations in every population the variation in progeny number, which was beyond experimenter's control, considerably reduced the effective population size below the actual number of parents used in each generation. Consequently, the means of variances of family size in almost half of the populations were close to or even larger than 2. This implies that generally, variance of family size in random-bred populations could be much larger than that of the Poisson distribution, and the formula Ne=4NM/(N+M) proposed by Wright (1938) over-estimates the actual effective population size.

V. FREQUENCY DISTRIBUTION OF LITTER SIZE

V.1. Abstract

The frequency distributions of 22422 observations on first parity litters of 8 control populations of mice of different origins, each maintained in two environments, were examined in this study. The distributions were all negatively skewed ($P<0.01$), indicating an excess of small size litters compared with normal distribution. All the distributions significantly deviated from normal, and the nonnormality of the distributions was greatly reduced by the power transformation of the type $Y'=(Y^k-1)/k$, and the k values ranged between 1.30 to 1.73. The populations that were maintained in the controlled environment had greater skewness and showed larger deviations from normality than their replicates maintained in an uncontrolled environment. The mean and variance of litter size in the replicates were significantly larger in almost half of the cases than those in the main populations. The larger mean litter size in the populations that were maintained in an uncontrolled environment and subjected to a faster rate of inbreeding compared with that in the populations maintained in the controlled environment, was rather unexpected and surprising.

V.2. Introduction

The description of the pattern of variability of litter size and its interpretation in terms of the underlying causes are the subject of this and the next chapter. Litter size was considered as the trait of choice in this study for several reasons. First; growth parameters (body weight and tail length at 21 and 42 days of age) were not recorded in all generations in each of the populations, while the data on reproductive traits were complete. Second; any finding regarding litter size would be more relevant to some problems in animal improvement, especially to such characters as the fertility of pigs, than traits such as female fertility or young mortality. Female fertility could not be studied because single pair mating was followed. Third; there are several detailed studies on the genetic control of litter size in mice, and on the effects of non-genetic factors on this trait, which facilitate interpretation of the results. Moreover, the components of litter size, namely ovulation rate and embryonic survival during the pre- and post implantation stages have also been the subject of several detailed studies.

Litter size is a very complex trait and is affected by numerous genetic and environmental factors many of which are difficult to evaluate. The complexity arises mainly from the fact that this trait is influenced by both parental and filial generations. In addition to the contribution of the female, it has been shown that genotype of the sire and fetus (Butler, 1958; Bishop, 1964; Finn, 1964; Swierstra and Dyck, 1976), and the interaction between sire and dam genotypes (Wakasugi *et al.*, 1967; Wakasugi, 1974) also influence the number of ova shed and the survival of the embryo in mice and pigs. It is very difficult to accurately describe the effects of genetic factors on litter size, yet some conclusions can be drawn from the results of experiments on the effects of inbreeding, crossbreeding and selection on litter size.

It has been demonstrated in several experiments that inbreeding has a negative effect (Bowman and Falconer, 1960; Falconer, 1960b; Roberts, 1960 McCarthy, 1967), and crossbreeding has a positive effect on litter size (Gruneberg, 1939; Eaton, 1941, 1953; Forsthoefel, 1954; Lyon, 1959; McCarthy, 1965; Bradford and Nott, 1969). It has been concluded from these experiments that some degree of dominance exists in the genes affecting litter size, the genes with negative effects are on the average recessive to their alleles that have positive effect, and there are recessive lethal genes which result in embryonic mortality. The availability of many inbred lines of mice whose litter sizes are as high as those in the non-inbred populations, and the absence of inbreeding depression in some lines under high rates of inbreeding (Bowman and Falconer, 1960; Falconer, 1960b, 1971; Eklund and Bradford, 1977) provide some indication that overdominance cannot be a major form of gene action controlling this trait. Directional dominance and deleterious recessives are then partly responsible for variation in litter size.

Based on the results of selection experiments it is possible to determine the relative amount of additive genetic variance. Different aspects of response to selection for litter size at birth in mice are reported by Falconer (1955, 1960b, 1965, 1971), Bateman (1966), Bradford (1968, 1969), Joakimsen and Baker (1977), Bakker *et al.* (1978) and Eisen (1978). The results of these experiments suggest that genes with additive effects are partly responsible for variation in litter size (shown by the realized heritabilities of less than 0.25). There are some indications (Joakimsen and Baker, 1977; Bakker *et al.*, 1978) that selection response is larger in populations that are genetically heterogeneous compared with populations with narrow genetic bases. In cases where selection was applied in both directions (Falconer, 1960b; Joakimsen and Baker, 1977) the realized h^2 of the low line was larger than that of the high line.

There have been several studies on the effects of inbreeding, crossbreeding and selection on the components of litter size in mice. Falconer (1960b) and Falconer and Roberts (1960) found that decrease in litter size as a result of inbreeding was due to an increase in pre-implantation mortality, and not due to a decrease in ovulation rate. Joakimsen and Baker (1977) and Falconer (1960b, 1963) reported that the main determinant of the increase in litter size in the high line was an increase in ovulation rate. Bateman (1966) and Bakker *et al*. (1978) reported that selection for large size litters resulted in simultaneous increase in ovulation rate and decrease in embryonic mortality. The decrease in litter size in low lines are reported to be due to increased embryonic loss (Falconer, 1963), or due to both a decrease in ovulation rate and an increase in embryonic loss (Joakimsen and Baker, 1977). From these findings, along with the results of inbreeding and crossbreeding experiments (Falconer and Roberts, 1960; Boshier, 1968; Bradford and Nott, 1969), and the study of Land and Falconer (1969) on selection for ovulation rate, it can be concluded that ovulation rate and embryonic mortality are probably controlled by different genes, and that ovulation rate seems to be controlled mainly by additive genes. There is evidence which shows that different genes affect pre- and post-implantation embryonic mortality, and that the genes affecting the former trait, exhibit a high degree of dominance. Embryonic death is generally influenced by recessive genes, some of which are deleterious and segregating at a low frequency in population.

Most of the methods used for statistical analysis are appropriate and efficient when models are structurally adequate (additivity of the components of the model and independency of the error terms), and data have constant variance and are normally distributed. These assumptions are and deleterious recessives are then partly responsible for variation in litter size.

Based on the results of selection experiments it is possible to determine the relative amount of additive genetic variance. Different aspects of response to selection for litter size at birth in mice are reported by Falconer (1955, 1960b, 1965, 1971), Bateman (1966), Bradford (1968, 1969), Joakimsen and Baker (1977), Bakker *et al.* (1978) and Eisen (1978). The results of these experiments suggest that genes with additive effects are partly responsible for variation in litter size (shown by the realized heritabilities of less than 0.25). There are some indications (Joakimsen and Baker, 1977; Bakker *et al.*, 1978) that selection response is larger in populations that are genetically heterogeneous compared with populations with narrow genetic bases. In cases where selection was applied in both directions (Falconer, 1960b; Joakimsen and Baker, 1977) the realized h^2 of the low line was larger than that of the high line.

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Most of the methods used for statistical analysis are appropriate and efficient when models are structurally adequate (additivity of the components of the model and independency of the error terms), and data have constant variance and are normally distributed. These assumptions are not, however, usually tested before employing a statistical methodology. Most of the theories in quantitative genetics are also based on the assumption that the phenotypic distributions are normal, and that the genetic and environmental components of phenotypic variation act additively and independently of one another (Falconer, 1981). Thus, inspection of the frequency distribution of any trait is helpful in recognizing the appropriate treatment that the data need to maximize the efficiency of the analysis.

Fisher *et al.* (1932) introduced statistical techniques for examining the shape of frequency distribution of a quantitative character, and pointed out that departure from normality could arise from environmental or genetic factors. Inappropriate environmental factors could sharply depress the performance of some individuals and would lead to a negative skewness. Non-additive genetic effects and selection could tend to act in a similar manner. The phenotypic distribution of quantitative traits which are under the influence of a major gene would also be skewed (Hammond and James, 1970).

The objective of this study was to investigate the effects of genetic heterogeneity and environmental conditions on the parameters (mean, variance, skewness, kurtosis) of the frequency distribution of litter size in populations of mice.

V.3. Statistical analysis

Data on 22422 first parity litters of 8 control populations of mice of different origins, each maintained in two environments, were used in this study. Infertile matings were not included, and litter size was defined as the total number of young born dead and alive at first parity. The only possible source of error in measuring litter size came from still-born young eaten by their mother before recording took place. The Kolmogorov-Smirnov one-sample test was used to compare the distributions of litter size with normal distribution. Homogeneity of distribution of litter size in the main and replicate populations were tested by the Kolmogorov-Smirnov two-sample test and by the Mann-Whitney U test. The Kolmogorov-Smirnov test is based on the differences between the cumulative distributions of the two groups which are being compared. This test is sensitive to any type of difference between the two distributions, such as median, dispersion and skewness. The Mann-Whitney U test ranks all the observations in order of increasing size and computes the test statistic U, the number of times a score from one group precedes a score from another group. If both groups have the same distribution, the distribution of the scores from the two groups in the ranked distributions will be random, an extreme value of U indicates a nonrandom pattern. When the number of observations is large (>30, as they were in the present study), the U is transformed into a normally distributed Z statistic.

The method of Box and Cox (1964) of shifted power transformation was used to find the most appropriate type of transformation for normalizing the data. The Box-Cox method gives the best type of transformation to normality within the family of power transformations. The transformation is in the following form (k is used instead of λ in the Box-Cox terminology):

$$Y' = (Y^k - 1)/k \text{ for } k \neq 0$$

$$Y' = \ln Y \text{ for } k = 0$$

When k=1, the distribution is normal, hence it is possible to test the hypothesis H_0: k=1 against H_1: k≠1 as the test for normality. The k=1/2 is equivalent to square root transformation, k=0 corresponds to the logarithmic transformation and k=-1 is equivalent to the reciprocal transformation. The values of k were computed from solving log likelihood functions by iterative procedure using an APL program. The Box-Cox algorithm also provides confidence limits for k. All computations were made by the SPSSX (1983) computer package unless specified otherwise.

V.4. Results

Normality of the frequency distributions:

The frequency distribution of litter size for each population is shown in Appendix V.1. The descriptive statistics of the litter size distribution of the populations pooled over all the generations, and the values for the main populations over the generations

Table V.1

Mean, phenotypic variance (V), skewness (G1) and kurtosis (G2) of litter size distribution of different populations

Pop.	No. of litters	Mean†	V†	Skewness G1	SE	Kurtosis G2	SE
QL	1649	9.81**	9.46	-.602	.060	.313	1.999
	(1392)‡	(9.82)**	(9.61)	(-.573)	(.066)	(.289)	(1.999)
QL-R	809	8.98	10.60	-.492	.086	-.254	1.998
LX	1608	9.37	6.68	-.553	.061	.508	1.999
	(1146)	(9.30)	(6.15)*	(-.693)	(.072)	(.806)	(1.998)
LX-R	580	9.15	7.13	-.390	.101	.356	1.997
NB	1421	8.92	6.35**	-.485	.065	.395	1.999
	(1095)	(8.87)	(6.15)**	(-.514)	(.074)	(.537)	(1.998)
NB-R	699	8.94	5.02	-.372	.092	.615	1.997
OC	1531	9.60**	7.25	-.569	.063	.489	1.999
	(1326)	(9.52)**	(7.18)	(-.561)	(.067)	(.553)	(1.999)
OC-R	806	10.28	7.43	-.473	.086	.555	1.998
AC	1471	8.56	5.63	-.588	.064	.467	1.999
	(1164)	(8.62)	(5.38)	(-.524)	(.072)	(.427)	(1.998)
AC-R	612	8.63	6.01	-.469	.099	.119	1.997
CD	1477	7.66**	5.12**	-.360	.064	.183	1.999
	(1180)	(7.55)**	(4.84)**	(-.305)	(.071)	(.170)	(1.998)
CD-R	708	8.31	6.22	-.545	.092	.000	1.997
IC	1628	8.30**	5.55**	-.611	.061	.440	1.999
	(1014)	(8.21)**	(5.34)**	(-.598)	(.077)	(.510)	(1.998)
IC-R	539	8.71	7.13	-.471	.105	-.134	1.996
GL	6196	10.30**	7.21**	-.839	.031	1.143	2.000
	(4728)	(10.42)**	(7.18)**	(-.895)	(.036)	(1.349)	(2.000)
GL-R	688	10.69	10.04	-.907	.093	.980	1.997

†-Significant difference between the main populations and their replicates are shown by ** (P<.01) and * (P<.05).

‡-Values in parentheses were computed over those generations of the main populations contemporaneous with their replicates.

contemporaneous with the replicates are shown in Table V.1. The distribution of litter size for all the populations showed significant negative skewness, indicating an excess of small and deficiency of large size litters compared with a normal distribution. All but three of the distributions were leptokurtic (positive kurtosis), but the coefficient of kurtosis was not significant in any of the cases, showing that some of the distributions tended to have more observations around their means compared with normal distribution.

The results of the Kolmogorov-Smirnov one-sample tests (Table V.2) indicated that all the distributions significantly deviated from a normal distribution. The magnitude of the coefficients of skewness and kurtosis and the Z values obtained from the Kolmogorov-Smirnov tests suggest that deviation from normality was generally more severe in the populations which were maintained in the controlled environment as compared with those kept in the uncontrolled environment.

The values of k obtained from the Box-Cox method of transformation and their 95% confidence intervals are presented in Table V.3. The fact that the confidence intervals did not include unity confirmed the results of the Kolmogorov-Smirnov one-sample tests that the distributions significantly deviated from normal in all the cases. The K values in all the replicates, except CD-R, were smaller than those in their corresponding main populations, indicating that the degree of deviation from normality was more severe in the latter. The maximum k value amongst all the populations, which indicates the largest degree of deviation from normality, was in the GL, followed by the GL-R. The confidence intervals indicated that the deviation of the GL population from normality was significantly larger than those in all other populations except GL-R and CD-R. The crosses between inbred lines had generally larger k values than those from non-inbreds in both environments, with the exception of the CD population.

The Box-Cox transformation resulted in a considerable improvement in the shape of distributions toward normality. The coefficient of skewness of the transformed data became much smaller than those of the original distributions, and all became insignificant except those for the GL and QL-R populations (Table V.3). The Kolmogorov-Smirnov test for the goodness of fit of the transformed data showed, however, that many of the distributions still significantly deviated from normal, but the Z values decreased to a large extent. The results of the Kolmogorov-Smirnov two-sample test and Mann-Whitney U test for the comparison between the distribution of litter size in the main populations and their replicates are shown in Table V.4. The distributions were significantly different from each other in all the cases except for the LX, NB and AC populations. The results of both test were consistent, although their algorithms were quite different.

Table V.2

The results of Kolmogorov-Smirnov one-sample test for normality of litter size distributions by population

Population	Largest difference	Z	Population	Largest difference	Z
QL	-.1203	4.88**	QL-R	-.1230	3.49**
LX	-.1207	4.84**	LX-R	-.1052	2.53**
NB	-.1327	5.00**	NB-R	-.1288	3.41**
OC	-.1175	4.60**	OC-R	-.1075	3.05**
AC	-.1358	5.20**	AC-R	-.1205	2.98**
CD	-.1177	4.52**	CD-R	-.1388	3.69**
IC	-.1435	5.79**	IC-R	-.1314	3.05**
GL	-.1402	11.12**	GL-R	-.1334	3.50**

** Significant at P<.01

Mean and variance of litter size:

Means of litter size distributions of the main populations were compared with those of their replicates by the two-tailed T-test for samples with unequal numbers and variances, and the results are shown in Table V.1. The means of litter size were significantly (P<.01) greater in the replicates compared with those in the corresponding main populations in the GL, OC, IC and CD, and were the same in all the other populations except QL which had larger average litter size than the QL-R (P<.01). The results did not change when only those generations in the main populations contemporaneous with the replicates were considered.

Variances of litter size were larger in the replicates than those in the corresponding main populations, and the differences were significant in the LX, CD, IC and GL populations. The only exception was the NB in which the variance of litter size was significantly ($P<.01$) larger than that in the NB-R (Table V.1). The ranking order of the main populations with respect to their phenotypic variance were QL> OC=GL=LX=NB> IC=AC=CD, showing a fairly good agreement between the expected genetic heterogeneity and total phenotypic variance in the controlled environment. Except for the NB-R, which had the smallest variance amongst all the populations, the ranking order of the replicates for their expected genetic heterogeneity and variance were the same.

V.5. Discussion

There was a high degree of correspondence between all the populations for the shape of the frequency distribution of litter size. Negative skewness in the distribution of litter size appears to be a common phenomenon in mice (Lyon *et al.*, 1964; Falconer, 1971; Joakimsen and Baker, 1977; Eisen, 1978). The frequency distributions of egg production in chickens, turkeys and ducks also have the same shape as that of litter size in mice (Clayton, 1975; Makarechian *et al.*, 1983). Hammond and James (1970) reported significant negative skewness and leptokurtosis for progeny number in *Drosophila melanogaster*. The Phenomenon of negative skewness of litter size distribution has received little attention in the literature. Inspection of such distributions are important from both analytical and quantitative genetic

Table V.3

Values of k† and their 95% confidence limits resulting from the Box-Cox transformation and the coefficients of skewness and kurtosis of the transformed distributions

		Confidence limits		Skewness		Kurtosis	
Pop.	k			Coef.	SE	Coef.	SE
QL	1.446	1.338	1.557	-.134	.060	-.117	1.999
QL-R	1.312	1.169	1.459	-.195	.068	-.451	1.998
LX	1.486	1.363	1.613	-.066	.061	-.024	1.999
LX-R	1.317	1.131	1.512	-.047	.101	.017	1.997
NB	1.423	1.295	1.555	-.057	.065	.058	1.999
NB-R	1.381	1.184	1.587	.001	.092	.183	1.997
OC	1.486	1.362	1.614	-.081	.063	-.102	1.999
OC-R	1.435	1.258	1.619	-.033	.086	.098	1.998
AC	1.524	1.393	1.659	-.081	.064	-.071	1.999
AC-R	1.439	1.232	1.652	-.079	.099	-.081	1.997
CD	1.300	1.179	1.423	-.054	.064	-.089	1.999
CD-R	1.478	1.292	1.671	-.140	.092	-.437	1.997
IC	1.532	1.409	1.657	-.094	.061	-.093	1.999
IC-R	1.407	1.195	1.626	-.129	.105	-.381	1.996
GL	1.727	1.660	1.794	-.089	.031	.135	2.000
GL-R	1.669	1.496	1.849	-.180	.093	-.027	1.997

†-Method of calculation defined in the text.

points of view. In this section, attempt will be made to discuss the relative importance of genetic and environmental factors in causing the phenomenon of negative skewness in litter size distribution.

Genetic control of litter size and the shape of its frequency distribution:

Negative skewness may result from the presence of a major gene affecting a metric trait (Hammond and James, 1970). There is no indication that litter size in mice or pig, or egg production in birds are influenced by such genes. Hammond and James (1970) analyzed the progeny number in *Drosophila*, and tentatively concluded that genes of large effect did not make a significant contribution to the variation of this trait. They found a power function of 2.5 as the best transformation for normalizing the distribution.

Negative skewness could result from segregation of many recessive deleterious genes which might cause high pre- and post-implantation mortality in some litters. Wright (1977) stated that a low rate of inbreeding, such as in progeny of first-cousin matings, typically gives rise to appreciable depression of mean of fitness traits but increases variability, mainly because of the extension of the lower tail of the phenotypic distribution due to increased segregation of deleterious recessive genes. Deleterious genes could not have been the only cause of skewness as the populations which had been originated from crosses between

Table V.4

Test of homogeneity of distribution of litter size in the main and replicate populations

Comparison	Kolmogorov-Smirnov test Z	Probability	Mann-Whitney U test Z	Probability
QL *vs* QL-R	2.45	0.00	-5.79	0.00
LX *vs* LX-R	1.02	0.25	-1.41	0.16
NB *vs* NB-R	0.91	0.38	-.22	0.82
OC *vs* OC-R	2.64	0.00	-6.31	0.00
AC *vs* AC-R	0.72	0.68	-.35	0.72
CD *vs* CD-R	4.11	0.00	-7.48	0.00
IC *vs* IC-R	2.49	0.00	-4.38	0.00
GL *vs* GL-R	2.49	0.00	-3.72	0.00

inbred lines (IC, AC, CD) also showed significant negative skewness. The inbred lines have been maintained by brother-sister or parent-offspring matings for many generations, and it is thus highly unlikely that they carry lethal genes, nor is it likely that many lethal genes, originating from new mutations, could segregate in appreciable frequencies in the crosses between inbred lines. The negative skewness in the litter size distribution of inbred lines of mice was also observed by Falconer (1971).

Distribution of a trait which is under the control of many recessive non-deleterious genes or genes with directional dominance is expected to be negatively skewed (Fisher *et al.*, 1932). The available information on the genetic control of litter size in mice suggest that both of these forms of gene action are controlling litter size and this may be a plausible explanation for the shape of the frequency distribution of this trait. Falconer (1971) reported that skewness of the frequency distribution of litter size in mice (live born litters, first parity) was greater in highly inbred lines than that in the crossbred progeny derived from them. He attributed the lower skewness of the distributions of litter size in the crossbred progeny to the suppressed expression of many recessive genes.

Fisher *et al*. (1932) pointed out that selection for high values of a variable, when applied to a symmetrical population, generally results in negative skewness. Conversely, selection for low values shift the skewness toward positive direction. The amount of change in skewness depends on the number of genes affecting the trait, the fewer the number of genes the higher the rate of change of skewness. There has been some selection for litter size in the history of QL, OC, and GL populations through the contribution of the JH population (high-litter size selection line of Dr. Falconer, see chapter II). Inevitably, some degree of selection for fitness traits has taken place during the formation of the inbred lines which were crossed to generate AC, CD and IC populations. It is unlikely that such selection pressures in the history of these populations could have caused the negative skewness of litter size distribution. Nevertheless, it seems logical to believe that a small selection force for fitness has been continuously applied to these populations, but such force has been operating towards an optimum value, which is not necessarily large size litters.

Comparisons between the frequency distribution of litter size in a control population of mice with those after 15 generations of two-way selection reported by Joakimsen and Baker (1977) seems to agree with Fisher's hypothesis. The distribution of litter size of mice at birth in the first three generations of a line subjected to selection for large litter size was negatively skewed, but the distribution became closer to normal as selection continued (Bakker *et al.*, 1978). On the contrary, Eisen (1978) reported that skewness of litter size distribution of a control population of mice was not significant, while skewness was significant in four populations subjected to long term selection for large litter size, large body weight, and indices composed of low litter size and high body weight and high litter size and low body weight. These conflicting observations may suggest that Fisher's hypothesis does not apply to the distribution of litter size in mice, and thus selection cannot be considered as a major cause of the negative skewness of the distribution of this trait.

It seems that the genetic control of litter size, namely the presence of directional dominance and seqregation of many recessive genes, explain, at least to some extent, the shape of its distribution. However, these factors do not explain why the distributions were closer to normal in the populations which were maintained in the uncontrolled environment (replicates), as the differences in the inbreeding coefficients between the populations cannot fully explain the observed differences. The explanation must be sought in the effects of environmental factors on litter size.

Environmental factors and the shape of litter size distribution:

The size of litter at birth is dependent upon harmonious effects of many underlying characters, each having a particular distribution, and each may respond differently to similar environmental conditions. The distribution of litter size consists of at least two major and almost discrete parts; the distribution of ova shed and the distribution of embryonic death (which can be further partitioned into pre- and post-implantation stages). It is well known that the number of ova shed in swine (Guthrie *et al.*, 1974; Swierstra and Dyck, 1976) and in mice (Lyon, 1959; McCarthy, 1965; Joakimsen and Baker, 1977) is in excess of the number of young born. Even if the distribution of ovulation rate is near normal, there are two major factors, accidental death of the embryo and uterus size, which may greatly influence the distribution of ovulation rate.

Embryonic mortality can be due to lethal or semi-lethal genes, as was considered before, or due to unknown environmental factors, i.e. accidental death. Accidental death is a random process depending so much on chance, but it may change the shape of litter size distribution if it is not evenly distributed over all litters. The experiment of Lyon *et al.* (1964) showed that dominant lethal genes induced by X-irradiation shifted the negatively skewed distribution of litter size toward a normal distribution. High rates of embryonic mortality during implantation stages in the irradiated samples increased the frequency of small size litters and decreased that of large size litters. Adverse environmental effects may have similar effect on litter size distribution. Clayton (1975) attributed the negatively skewed distribution of egg production in poultry to accidental losses of ova shed.

Limitation imposed by the size of uterus could also truncate the normal variability of the number of ova shed during and after the implantation process, and the effect of this force would be more pronounced when the number of ova shed is large. It has been demonstrated in mice (Bowman and Roberts, 1958; Carter and Lyon, 1961; Bateman, 1966; Guthrie *et al.*, 1974), and in pigs (Guthrie *et al.*, 1974; Swierstra and Dyck, 1976), that females shedding large numbers of eggs have a higher rate of embryonic mortality, which could cause the distribution of litter size to be negatively skewed.

Statistical implication of litter size distribution:

Despite the great deal of improvement in the coefficient of skewness of the litter size distribution in all the populations by applying the Box-Cox transformation, many of the distributions still remained significantly different from normal. This somewhat confirms the remark that "normality is a myth, there never was, and never will be a normal distribution" (Mardia, 1980). The normal distribution has always been the most widely assumed distribution, since this assumption leads to a rich set of mathematical consequences. However, just as important as normal theory is, so it is important to know when, and to what extent, a distribution is departing from the state of normality. It is also possible that the deviations of the transformed distributions from normality, despite insignificant coefficients of the third and fourth moments, were due to the high sensitivity of the Kolmogorov-Smirnov goodness of fit test.

Transformation did not change the significance levels in analyses of variance or regression analyses (the results will be discussed in the next chapter). Davies (1967) suggested that small deviations of skewness and kurtosis from the values in normal distribution did not seriously affect significance levels in analyses of variance. The results are in agreement with the assumption made by Roberts (1965) that distribution of litter size is sufficiently close to normal for most statistical tests to be valid without transformation.

Quantitative genetic theory and distribution of litter size

Negative skewness of litter size distribution would result in over-estimation of expectation from selection compared to normal distribution. A basic assumption in estimating heritability is that the regression of genetic value on phenotypic value is linear (Abplanalp, 1961; Falconer, 1981). It has been shown (Nishida and Abe, 1972) that skewed genetic or phenotypic distributions could result in curvilinear regression of genotype on phenotype, i.e. curvilinear heritability.

Mean and variance of litter size

A rather surprising result was that the mean litter size in only one of the replicates (QL-R) was significantly smaller than that in the corresponding main population. The replicates were maintained under a rather harsh environment with smaller population size which resulted in faster rate of inbreeding compared with the main populations. Yet these populations somehow managed to keep their average litter size larger or equal to that of the main populations. The frequency distributions of litter size (Appendix V.1) reveal that the mode class in the GL-R, OC-R, AC-R and CD-R, and the maximum litter size in the GL-R, OC-R, AC-R and IC-R populations were larger than those in their corresponding main populations. The larger mean litter size in the GL-R, OC-R, IC-R and CD-R compared with that in their main populations is therefore the result of higher frequency of the larger litters.

Studies with laboratory populations of *Drosophila* have shown that the rate of loss of heterozygosity at a number of allozyme loci is retarded in the more variable environment (Powell, 1971; McDonald and Ayala, 1974). Positive association between environmental heterogeneity and genetic heterozygosity were also reported by Dempster (1955), Beardmore and Levine (1963), Haldane and Jayakar (1963), Gillespie and Langley (1974), Gillespie (1976) and Mackay (1981). It has been suggested (Felsenstein, 1976) that environmental heterogeneity is sufficient to maintain genetic variability. There is evidence which indicates that the positive association between genetic heterogeneity and environmental variability is likely due to higher fitness of the heterozygote individuals by virtue of their superior biochemical flexibility, which makes them developmentaly more stable (Lewontin, 1958; Mackay, 1980). It may be hypothesized that the amount of heterozygosity in the replicates was higher than what is indicated by their inbreeding coefficient, and that the amount of heterozygosity in the replicates might have been higher than that in the main populations. If this hypothesis is true, the larger means of some of the replicates could be attributed to their higher degree of heterozygosity.

Automatic selection was avoided insofar as possible by selecting two individuals from each litter. However, since some small size litters contributed only one sex, and occasionally only one individual was born, some selection for large litter size has inevitably taken place. Automatic selection could have been more effective in increasing the litter size in the replicates than in the main populations on the account of their larger variance. Bray *et al.* (1962) observed that the variance of pupae weight in *Tribulium* was two times greater in the harsh environment (dry) than that in a more favourable environment (wet), and attributed the faster response to selection for pupae weight in the former to the greater phenotypic variance. A similar situation could have been present in this study in which natural selection was the acting force. It is not, however, clear why the means of litter size in some of the replicates were the same or below that of the main populations, as there was not any association between the differences in the performance of the main and replicate populations in the two environments and their expected genetic heterogeneity.

The significantly smaller variance of the NB-R than the NB was most likely due to its genetically narrow bases, as this population originated from a family of full-sibs (see Chapter II).

VI. VARIATIONS OF LITTER SIZE

VI.1. Abstract

There were significant differences in litter size among generations in almost all the populations. A fairly good agreement existed between the expected genetic heterogeneity of the populations and their within generation mean-squares, i.e. the crosses between inbred lines had generally smaller within generation mean-squares compared to the non-inbred populations. The trends of litter size by generation were highly variable in different populations, ranging from positive and highly significant to negative and highly significant. The negative trends were not likely due to inbreeding depression alone, as the pooled linear regression coefficients of litter size on percent inbreeding were insignificant in most of the populations. In addition, decreases in litter size by generation were generally due to either a sudden change in the linear trend or discontinuity of the regression lines at some generations, i.e. mean litter size stayed stable over several generations, showed a sharp decline in one generation, and did not return to the original level afterwards. There was no clear relationship between the genetic heterogeneity of the populations and their trends with respect to inbreeding or generation number. Time series analysis showed that there were patterns in the fluctuation of mean litter size from generation to generation in most of the populations, but the patterns were

not consistent across the populations. The results suggested that neither the fluctuations nor the trends of mean litter size over generation could be fully attributable to the environmental variations, and therefore the genetic constitution of the populations might have also influenced the patterns of variation and the trends.

VI.2. Introduction

Control populations could be useful in practical animal breeding at least in two areas, namely selection experiments and conservation of genetic resources. One of the problems in selection programs is to accurately separate environmental and genetic variations in order to measure genetic changes resulting from selection. Keeping a control population is one of the available methods to overcome this problem, especially in small-size species such as poultry or laboratory animals. In other words, a stable control population is used as a bench mark from which it is possible to measure genetic changes in the population under selection. The difference between the performance of the control and selected group, both maintained in the same environment at the same time is then an estimate of genetic change in the selected group. Control lines have been extensively used in selection experiments with laboratory animals, even though selected groups in laboratory animals are generally kept in well regulated environmental conditions which help to minimize trends or random fluctuations in performance from generation to generation. Control populations have been used more extensively in poultry and swine selection experiments than in larger species of farm animals where other techniques had to be used because of high costs. Hill (1972b) reviewed many papers and concluded that control populations had been generally useful in fulfilling their expected objective.

Another application of control population is in planning breeding programs for conservation of the genetic resources. For many years, the most important issue which concerned animal breeders was to increase the productivity of different species of farm animals. Through application of genetic principles and proper management techniques, high levels of productions with a great degree of specialization have been achieved in farm animals. These rapid genetic improvements have been achieved at a considerable cost, namely decline or loss of irreplaceable genetic materials, which have evolved over many thousand years under natural and artificial selection in various environmental conditions. The number of breeds are declining and, at the same time, owing to intensive selection for a few production traits, the genetic base of the surviving breeds seems to becoming restricted. Disappearance of the locally adapted breeds in developing countries and their replacement with exotic ones is not surprising, as the importation of high-yielding breeding materials from the developed countries for increasing production levels has been widely used (Deaton, 1981; Osman, 1981; Rendel, 1981). Disappearance of genetic materials is becoming a matter of concern even in the developed countries (Maijala *et al.*, 1984; Simon, 1984). For example, twenty three breeds of livestock have become extinct in Britain since the turn of the century and fifty five breeds of large livestock are now listed as rare (Alderson, 1981). Most of the current attention in developed countries continues to be toward further improvement of a few specialized breeds, or on the use of these breeds for crossbreeding purposes. Breeds having a lower total productivity or not suitable for intensive type of production, have been quickly replaced by some which are more productive and specialized (Colleau *et al.*, 1982; Ordonez, 1982; Cunningham, 1983).

The loss of genetic materials occurs as a result of change in production systems and conditions under which the animals are maintained. It would be difficult to accurately predict the conditions under which the animals will be raised far in the future. The emphasis for conservation of "valuable breeds" has changed to conservation of "all genetic materials" these days, because the importance and value of a breed will change over years. The need for conservation of genetic materials has been well recognized (Jaap, 1965; Scossiroli, 1965; Maijala *et al.*, 1984; Phillips, 1974; Simon, 1984; Smith, 1984). In recent years, some organizations have emerged with the objective of maintaining the rare or commercially unimportant local breeds. The Rare Breed Survival Trust of Britain (Alderson, 1981), National Bureau of Animal Genetic Resources of India (Swaminathan, 1981), and similar organizations in Bulgaria (Hinkovski and Alexiev, 1981), Canada (Crawford, 1981, 1982, 1983), Italy (Rognoni and Finzi, 1984) and Spain (Campo and Orozco, 1982) are now functioning. FAO is also playing an active role in developing countries in this respect (Rendel, 1982).

Although new techniques, such as freezing the germ plasm, are becomming available for the conservation of genetic resources; maintaining a living sample with the intention of keeping its initial genetic variability has certain advantages. The possibility of increased variability by mutation, achieving higher level of adaptation by natural selection, achieving more appropriate breed evaluation, and maintaining interest in the breed are among the advantages (Maijala *et al.*, 1984). Wild animals in their own habitat and in the zoos have to be maintained in the form of live samples. Maintaining a sample of a population, for either selection or conservation programs, share common features and similar technical problems. These problems include the genetic structure of the original population, sample size and breeding method to attain maximum genetic stability with minimum operational cost. Therefore, theories which have been proposed for the former (Gowe *et al.*, 1959b; Hill, 1972a) are basically the same as those suggested for the latter purpose (Crawford, 1981; Yamada, 1981; Smith, 1984;

Yamada and Kimura, 1984). The general consensus is that inbred lines have a constant genetic structure over generations, but one or a few of such lines at best represent only a narrow range of genetic variability of a population, and it is not practical to easily create many inbred lines in every species. Control lines must be closely related to the lines undergoing selection, and it is desirable to initiate a selection program in a population which has a broad genetic base in order to achieve rapid selection response. Similarly, the original genetic variability of any gene pool maintained for the conservation of genetic resources should be as large as possible. However, the larger the genetic variability of a population, the greater the likelihood of genetic drift under any particular population size and mating system. Despite much theoretical work on the effects of genetic heterogeneity and size of population on genetic and phenotypic stability of control populations, long-term performance of control populations with different original genetic heterogeneity, particularly in laboratory mammals, has not been studied in any experiment. The present data provide a unique opportunity for such an investigation.

Studying several control populations with different original genetic heterogeneity, each maintained in two environments for many generations could throw some light in understanding the evolutionary process by which organisms have been brought to their present state of organization and adaptation. The evolutionary process in nature is the net result of numerous, difficult to measure, and interacting forces. It would be impossible to consider even a small fraction of such forces in any experiment. One route open to the investigator is to hold all but one or two of the known forces as constant as possible. However, a high degree of precision in understanding the patterns of variation would be highly unlikely in such an over-simplified situation. Nevertheless, any observed phenomenon resulting from studying several control populations would be valuable as it could be helpful in the interpretation of the changes occuring in natural populations.

The main objectives of the analyses performed in this section were:

i- To study the patterns of variation of litter size and its trends with respect to inbreeding and generation number.
ii-To search for probable observable phenomena.
iii-To interpret the findings with regard to the available knowledge on genetic control of litter size, and with respect to genetic heterogeneity of the populations and environmental conditions.

VI.3. Statistical analysis

Differences between mean litter size over generations within each population was tested by one-way analysis of variance. Between generations component of variance (σ^2b) was estimated as

$$\sigma^2 b=[(\text{Between generations mean-squares}) -(\text{within generations mean-squares})]/k,$$

where k is the harmonic mean of the number of observations per generation ($n_{i.}$) over "s" generations:

$$k=[\sum_{i=1}^{s} n_{i.} -(\sum_{i=1}^{s} n_{i.}^2/\sum_{i=1}^{s} n_{i.})]/(s-1)$$

Inbreeding depression ($\bar{b}$) was estimated by pooling the sum of squares and crossproducts of each of the "s" generations (Sokal and Rohlf, 1981):

$$\bar{b} = \sum_{i=1}^{s}\sum_{j=1}^{n} xy/\sum_{i=1}^{s}\sum_{j=1}^{n} x^2$$

Standard error of the pooled regression coefficient was computed as:

$$\{\{\sum_{i=1}^{s}[\sum_{j=1}^{n} y^2 -(\sum_{j=1}^{n} xy)^2/\sum_{j=1}^{n} x^2]/ (\sum_{i=1}^{s} n_{i.}-2s)\}/\sum_{i=1}^{s}\sum_{j=1}^{n} x^2\}^{0.5}$$

The homogeneity of within generation regression coefficients was tested by the F statistics using the following parameters (Sokal and Rohlf, 1981):

Among b's sum of squares= $\sum_{i=1}^{s}[(\sum_{j=1}^{n} xy)^2/\sum_{j=1}^{n} x^2] -\sum_{i=1}^{s}\sum_{j=1}^{n} x^2$ which has s-1 degrees of freedom.

Weighted average of deviations from regression lines=

$$\sum_{i=1}^{s}[\sum_{j=1}^{n} y^2 -(\sum_{j=1}^{n} xy)^2/\sum_{j=1}^{n} x^2]$$

with $\sum_{i=1}^{s} n_{i.}-2s$ degrees of freedom. Pooled regression coefficients, their standard errors and tests for homogeneity of regression coefficients were performed by use of a FORTRAN program. Cochran's C and Bartlett-Box F tests were used to check the homogeneity of variances.

Stability of litter size over generations was tested by regressing the individual litter size and mean of litter size in each generation on generation number, using a polynomial of degree five by stepwise regression procedure. In order to detect the presence of any pattern in the fluctuation of litter size from generation to generation, the runs test and time-series analysis (Box and Jenkins, 1976) were used. Probable appropriate models were selected by examining the autocorrelation and partial autocorrelation coefficients. Such models were fitted to the data and the most appropriate one was selected based on the behavior of the residuals. When series was not stationary, the first difference of the original data was taken, and the resultant series was reanalyzed. Some information about the time series analysis is presented in Appendix VI.2. All statistical analyses were made using the SPSSX (1983) program unless specified otherwise.

VI.4. Results

Variation of litter size over generations:

The plots of the mean litter size by generations are illustrated in Appendix VI.1, and the limits of fluctuation of mean litter size are shown in Table VI.1. The limits of fluctuation of mean litter size per generation in the main populations ranged from 2.24 to 3.83, and the limits were farther away in the replicates, ranging from 3.53 to 5.18. It is interesting to note that the wider ranges of the fluctuations in the replicates compared with those in the main populations were not due only to the smaller minimum values but also due to the larger maximum values of the mean litter size of the former group. In fact, the plots in Appendix VI.1 show that, with few exceptions, mean litter size in many generations in the replicates was larger than the maximum mean value in their corresponding main populations. This phenomenon was particularly apparent in the OC, CD, and GL populations. There was no general correspondence between the expected genetic heterogeneity of the populations and the differences between the two limits within which the generation means fluctuated.

The results of the one-way analysis of variance, between generation component of variance (σ^2b) and between generation component of variance as percentage of the within generation component of variance (100 σ^2b/σ^2w) are presented in Table VI.2. Significant differences existed between generations for litter size in all the populations, except for the QL-R. There was no easy way to explain the relationship between the expected genetic heterogeneity of the populations and their between generations mean-squares or σ^2b, while the main and replicate populations originating from crosses between inbred lines generally had smaller within generations mean-squares. Amongst the main populations, σ^2w was the smallest in the crosses between inbred-lines, intermediate in the LX and NB and the largest in the GL, OC and QL populations, indicating a fairly good agreement between the genetic heterogeneity of the populations and their σ^2w. The ranking order for the genetic heterogeneity and σ^2w in the replicates was almost similar to that of the main populations, except for the NB-R which had the smallest σ^2w of all the populations and the IC-R which had larger σ^2w than the LX-R and NB-R. The population QL-R was the only one whose within generation mean-square was larger than its between generation mean-square, resulting in a negative σ^2b which was considered to be an estimate of zero.

The difference in the environmental conditions under which the main populations and their replicates were raised and the differences in population size did not have a consistent effect on the magnitude of σ^2w, as these values in some of the main populations were larger than the corresponding values in their replicates, while the opposite was true in some others. The σ^2b's in the replicates were larger than those in the main populations, except for the QL and CD populations. Since total phenotypic variance (column 4, Table V.1) is equal to $\sigma^2b+\sigma^2w$, the results indicate that the larger phenotypic variance of litter size in the replicates compared with that in the main populations was partly due to their larger σ^2b, and the smaller total phenotypic variances of the crosses between inbred lines compared with those in the non-inbred populations in the controlled environment was largely due to their smaller σ^2w. The estimates of σ^2b, although significant, were a small

Table VI.1

The generations in which the mean litter size was maximum or minimum within each population

	Minimum		Maximum		
Pop.	Gen.	Mean	Gen.	Mean	Range
QL	7	8.21	49	12.04	3.83
QL-R	61	7.27	54	10.80	3.53
LX	57	7.88	1	11.21	3.33
LX-R	70	6.55	26	11.73	5.18
NB	38	7.25	5	11.00	3.75
NB-R	56	6.60	21	11.15	4.55
OC	64	7.96	16	11.50	3.54
OC-R	63	8.43	38	12.00	3.57
AC	8	6.82	3	10.20	3.38
AC-R	56	6.20	38	10.47	4.27
CD	56	6.14	1	9.90	3.76
CD-R	52	6.17	19	10.29	4.12
IC	15	6.95	61	9.88	2.93
IC-R	52	4.67	20	10.40	5.73
GL	2	8.87	16	11.11	2.24
GL-R	67	8.20	21	12.67	4.47

fraction of $\sigma^2 w$, ranging from 1.65% in the GL to 8.66% in the CD amongst the main populations, and from zero in the QL-R to 21.16% in the LX-R in the replicates.

The between generations component of variance was much smaller than the variance of the observed generation means ($\sigma^2 m$) in all the populations, as shown in Table VI.3. Difference between these two parameters is attributable to the sampling variance ($\sigma^2 s$), which is expected to be $1/k\sigma^2 w$, where k is the harmonic mean of the number of litters per generation (values of k are shown in Table VI.2). The variances of observed generation means were very close to the $\sigma^2 b+\sigma^2 s$ in all the populations (Table VI.3), indicating that the variance of observed generation means was fully accounted for by the true between generation variance (σ^2b) and the sampling variance (σ^2s). The σ^2b's were generally smaller than the σ^2s's in the main populations, but the reverse was true in the replicates. Thus the larger variances of observed generation means in the replicates compared with those in the main populations were not entirely due to their smaller sample sizes.

Stability and inbreeding depression:

The effects of any directional change in the environmental conditions over generations were highly confounded with the effects of inbreeding, as the correlation coefficients between these two independent variables were high in all the populations. The high degree of colinearity between the inbreeding coefficient and the generation number resulted in:

i-Levels of significance of the regression coefficients of litter size on generation number and on percent inbreeding coefficient were the same, and the R^2 values of the two regressions were very close to each other, as illustrated in Table VI.4.

ii-Adding the inbreeding coefficient as an independent variable to the regression models did not change the value of R^2 when the generation number was already in, and *vice versa*.

iii-In cases where the regression coefficients of litter

Table VI.2

One-way analysis of variance of litter size by generation and population

	Between gen.		Within gen.					
Pop.	d.f.	MS†	d.f.	MS†	Sig. level	k‡	$\sigma^2 b$	$100\sigma^2 b/\sigma^2 w$ ¶
QL	71	16.52	1577	9.15	.000	22.9	0.323	3.53
QL-R	58	9.33	750	10.70	.739	13.7	-.099	0.00
LX	72	9.25	1535	6.56	.015	22.0	0.122	1.86
LX-R	49	20.39	530	5.91	.000	11.6	1.250	21.16
NB	72	10.89	1348	6.11	.000	19.4	0.246	4.03
NB-R	53	13.21	645	4.32	.000	12.9	0.687	15.92
OC	68	12.92	1462	6.99	.000	22.2	0.268	3.84
OC-R	58	15.16	747	6.83	.000	13.7	0.610	8.93
AC	68	7.80	1402	5.53	.017	21.3	0.107	1.94
AC-R	50	12.74	561	5.42	.000	12.0	0.610	11.26
CD	68	13.46	1408	4.72	.000	21.4	0.409	8.66
CD-R	52	11.01	655	5.84	.000	13.4	0.387	6.63
IC	68	8.27	1559	5.43	.004	23.6	0.120	2.21
IC-R	41	14.92	497	6.49	.000	12.8	0.658	10.14
GL	66	18.12	6129	7.10	.000	93.9	0.117	1.65
GL-R	49	13.52	638	9.78	.046	13.8	0.272	2.78

† Mean-square.
‡ Harmonic mean of the number of litters per generation.
¶ $\sigma^2 b$ and $\sigma^2 w$ are between and within generations components of variance.

Table VI.3

Variance of observed generation means (σ^2m), sampling variance (σ^2s), σ^2b+σ^2s, and σ^2b† as percentage of σ^2s

Pop.	σ^2m	σ^2s	σ^2b+σ^2s	100σ^2b/σ^2s
QL	0.724	0.400	0.723	81.0
QL-R	0.669	0.780	0.780	0.0‡
LX	0.450	0.298	0.420	40.9
LX-R	1.740	0.510	1.760	245.1
NB	0.607	0.314	0.560	78.3
NB-R	1.044	0.334	1.021	205.7
OC	0.579	0.315	0.583	85.1
OC-R	1.105	0.500	1.110	122.0
AC	0.410	0.259	0.366	41.3
AC-R	1.057	0.452	1.062	134.9
CD	0.684	0.221	0.630	185.1
CD-R	0.837	0.437	0.824	88.6
IC	0.366	0.230	0.350	52.2
IC-R	1.462	0.506	1.164	130.0
GL	0.207	0.076	0.193	154.8
GL-R	0.966	0.710	0.982	36.3

† σ^2b=between generation component of variance.
‡ The estimate of σ^2b was negative and it was assumed to be zero.

size on the generation number and on inbreeding coefficient were significant when they were used separately, the standard error of the coefficients became large and the regression coefficients became insignificant when both variables were simultaneously forced into the regression models (unstable regression coefficient).
Therefore, the effect of one independent variable after the other was basically nil.

One method for estimating the change of a trait by inbreeding in such cases would be to study all the within subclasses regressions. In cases where this method was applied in farm animals (Tebb, 1958; Morris, 1962; Kinney *et al.*, 1968), the number of subclasses (year, generation, etc.) had not been very large. In the present study, all the within generation linear regressions (a total of 975) were computed and part of the results are presented in Table VI.5. Only a small percentage of the within generation regression coefficients in each population were significant. The within generation regression coefficients were homogeneous in all the populations. Test of homogeneity of the within generation regressions showed that both the among regressions mean square and the weighted average deviations from the regression lines in the crosses between inbred lines which were maintained in the controlled environment were smaller than the corresponding values in the other populations (Table VI.6). This suggests that the within generation regression lines were more homogeneous and the observations had smaller deviation from the regression lines in the crosses between inbred lines as compared with the other populations. The among regression mean squares in the main populations were generally smaller than those in the replicates, showing that the variations among the within generation regression lines in the former were less than that in the latter group. The within generation regression coefficients were regressed on generation number to see if they showed any trend over time, and the results are shown in Table VI.5. In no case was there any detectable trend in inbreeding depression per generation over the course of the study, except for the GL population in which the inbreeding depression became more severe as the population was kept longer.

It was almost impossible to make any conclusion from the very large number of the regression coefficients, and thus the pooled estimate of the regression coefficients was computed. This method is useful in removing variation between the subclass means and has been used in farm animals and poultry (Tebb, 1958; Gowe *et al.*, 1959a; Swiger *et al.*, 1961; Morris, 1962) and in laboratory animals (Eisen, 1978). In pooling any set of data, however, the question of homogeneity of variances and regression coefficients from the separate subclasses needs to be considered. Statistical tests confirmed the homogeneity of the regression coefficients, but significant heteroscedasticity was observed in the data (Table VI.6). Cochran's test indicated the presence of heteroscedasticity in only six populations, but the Bartlett-Box method indicated the presence of heteroscedasticity in all but one of the populations, which might lead to some biasedness in the pooled parameters.

The pooled linear regression of litter size on percent inbreeding of progeny are shown in Table VI.6. Even though the within generation regression coefficients of litter size on percent inbreeding of the progeny and dam were not the same in each generation, nevertheless, the pooled regressions were close to each other and so only the latter are presented. The populations responded quite differently to the increase in inbreeding coefficient. The pooled regression coefficients ranged from -.163 to +.052 young per 1% increase in the inbreeding coefficient but were not significantly different from zero, except for the LX, CD and OC-R ($P<0.05$), and for IC-R and GL-R which approached significance level ($P<0.10$). There was no correspondence between the expected genetic heterogeneity of the populations or environmental conditions and the magnitude and direction of the pooled regression coefficients. Also presented in Table VI.6 are the total amount of inbreeding depression based on the pooled regression coefficients and the increase in inbreeding coefficient over the course of the study. These estimates were generally much larger than what were observed from the regression of litter size on generation number which are also illustrated in the same table.

Table VI.4

Linear regression of individual litter size on generation number and on percent inbreeding coefficient of the progeny by population

	Generation number			% inbreeding		
Pop.	β±SE	%R²	P†	β±SE	%R²	P†
QL	+.00302±.00368	0.04	0.41	+.00300±.00590	0.02	0.61
QL-R	-.01088±.00674	0.32	0.10	-.01422±.00857	0.34	0.10
LX	-.00831±.00308	0.45	0.00	-.01252±.00438	0.51	0.00
LX-R	-.06085±.00724	10.90	0.00	-.06807±.00818	10.69	0.00
NB	-.01588±.00314	1.78	0.00	-.01256±.00325	1.04	0.00
NB-R	-.04109±.00506	8.65	0.00	-.06512±.00820	8.29	0.00
OC	-.02431±.00340	3.24	0.00	-.03943±.00553	3.21	0.00
OC-R	-.02231±.00557	1.96	0.00	-.02657±.00689	1.82	0.00
AC	+.00477±.00329	0.15	0.14	+.01245±.00945	0.12	0.19
AC-R	-.02201±.00664	1.77	0.00	-.03980±.01274	1.57	0.00
CD	-.02851±.00305	5.60	0.00	-.08777±.00968	5.27	0.00
CD-R	-.02983±.00586	3.53	0.00	-.06974±.01376	3.51	0.00
IC	+.00217±.00298	0.03	0.47	+.00255±.00601	0.01	0.67
IC-R	-.05377±.00932	5.83	0.00	-.06008±.00967	6.71	0.00
GL	+.01008±.00177	0.52	0.00	+.04317±.00778	0.49	0.00
GL-R	-.02759±.00827	1.60	0.00	-.03260±.00924	1.78	0.00

† Significance level.

Table VI.5

Percentage of significant within generation regressions (β_i), test for homogeneity of β_i's, and the regression of β_i's on generation number by population

	% Significant β_i		Homogeneity of β_i‡		Trend of β_i's on generations
Pop.	Positive slope	Negative slope	Among M.S.	Within M.S.	$\beta \pm SE$
QL	2.8	2.8	8.78	9.19	+.0057 ± 0.0044
QL-R	5.1	3.4	10.15	10.73	+.0008 ± 0.0057
LX	2.8	2.8	6.12	6.58	+.0036 ± 0.0022
LX-R	4.0	4.0	6.77	5.83	-.0061 ± 0.0088
NB	0.0	2.8	5.80	6.01	+.0018 ± 0.0036
NB-R	1.9	1.9	4.02	4.36	+.0023 ± 0.0071
OC	4.3	5.8	8.80	6.90	+.0024 ± 0.0034
OC-R	3.4	6.8	8.93†	6.61	+.0053 ± 0.0064
AC	0.0	1.5	4.33	5.59	-.0009 ± 0.0043
AC-R	5.9	5.9	6.24	5.34	-.0065 ± 0.0194
CD	0.0	7.5	4.96	4.70	+.0022 ± 0.0049
CD-R	3.0	7.6	5.92	5.83	+.0108 ± 0.0129
IC	0.0	1.4	4.06	5.44	-.0065 ± 0.0038
IC-R	2.4	4.8	8.60†	6.26	+.0188 ± 0.0243
GL	1.5	7.5	8.29	7.08	-.0083 ± 0.0025*
GL-R	0.0	2.0	7.98	9.89	+.0012 ± 0.0088

Significance levels are shown by ** ($P<0.01$), * ($P<0.05$) and † ($P<0.10$).

‡ Among M.S. and within M.S. are among regressions mean squares and weighted average of deviations from regression lines respectively (see the text for calculation methods).

Table VI.6

Pooled linear regression of litter size on percent inbreeding coefficient, estimated total inbreeding depression (ID)‡, total decline in litter size over generations (GD)¶, and tests of homogeneity of within generation variances by population

Pop.	β±SE	ID	GD	Cochran C	Bartlett-Box F
QL	+.0523 ± 0.0457	+2.53	+.21	.026	1.69**
QL-R	-.0832 ± 0.0647	-4.57	-.64	.033	1.04
LX	-.0648 ± 0.0333*	-3.78	-.61	.034*	1.47**
LX-R	-.0405 ± 0.0733	-2.67	-3.04	.061*	1.38*
NB	+.0174 ± 0.0432	+1.22	-1.16	.043**	1.94**
NB-R	-.0023 ± 0.0731	-.17	-2.22	.056*	1.39*
OC	-.0282 ± 0.0398	-1.20	-1.68	.026	1.31*
OC-R	-.1420 ± 0.0601*	-7.56	-1.32	.038	1.71**
AC	-.0306 ± 0.0702	-1.55	+.33	.032	1.39*
AC-R	-.0733 ± 0.1135	-4.63	-1.12	.045	1.40*
CD	-.1301 ± 0.0634*	-7.53	-1.97	.030	1.38*
CD-R	-.1260 ± 0.1303	-7.65	-1.58	.055*	1.80**
IC	+.0203 ± 0.0447	+.95	+.15	.031†	1.888*
IC-R	-.1634 ± 0.0858†	-10.02	-2.26	.069*	1.60**
GL	-.0153 ± 0.0238	.021	-.25	.67	1.81**
GL-R	-.1270 ± 0.0740†	-5.96	-1.38	.041	1.61**

Significance levels are shown by ** (P<0.01), * (P<0.05) and † (P<0.10).

‡ (Pooled regression coefficient) x (total increase in inbreeding coefficient over the course of the study).

¶ (Regression coefficient of litter size over generations) x (generation number).

The linear regression of litter size on generation number was negative and significant (P<0.01) in most of the populations (Table VI.4). The exceptions were the QL-R in which the regression coefficient was negative but insignificant (P=.10), and the QL, AC, IC and GL populations in which the regression coefficients were all positive, but significant only in the GL. There was no relationship between the genetic heterogeneity of the populations and the direction and the magnitude of the trends of litter size with respect to generation. The R^2 values were generally small because the individual litters had a large degree of variation within each generation. The results of regressing mean of litter size in each generation on generation number were close to the estimates obtained when individual observations were used, but the coefficients of determination were larger, as expected.

The regression equations best describing the association between litter size and generation number were not linear in many of the populations. Polynomial regressions explained larger portion of the variation in such cases than did the linear equations. However, differences in R^2 between the polynomial and linear regressions were generally small, and the inspection of the residual plots suggested that even the polynomial regressions fitted the data poorly in most cases. The logarithmic and reciprocal transformations were also used, but they failed to linearize the regression functions. The plots of mean litter size by generations (Appendix VI.1) showed that most of the populations exhibited either a sudden change in mean litter size in one or over a few generations (discontinuous regression), or had a drastic change in linear trends in some generations. No polynomial regressions were capable of explaining the patterns and no transformations could linearize such variations. Piecewise linear regression (Neter and Wasserman, 1974) was found to be a more appropriate analysis. Several generations within each population in which a linear trend was changed or discontinued were identified by inspecting the plots (Appendix VI.1), and piecewise regressions were employed by defining appropriate indicator variables. The function which best fitted the data, judged by R^2 values and behavior of the residuals, were identified. Linear regressions were then fitted to each period to test the significance of the regression coefficients.

In case changes in the environmental conditions had caused the sudden changes in the mean litter size with temporary or permanent effects, then they should have had the same effect on all the contemporaneous populations. A detailed study of the behavior of the mean litter size over generations in different populations would therefore be helpful in identifying the sources of variation of litter size. Because of the differences in the environmental conditions under which the main populations and the replicates were maintained, each group were considered separately.

The mean litter size in the OC, LX, and NB populations remained stable over several generations, declined sharply during a few generations, and stayed below the original levels for the remaining generations. The mean litter size decreased almost consecutively from 10.54 in generation 23 to 8.27 in generation 29 (pairing dates extended from 1968/050[*] to 1969/140) in the OC population, and stayed low afterwards. The linear regression coefficients for the two periods were:

Generations 1 to 24 β=+.01305±.01621 (P=.43)

Generations 25 to 69 β=-.00595±.00587 (P=.32)

In the NB population, the mean litter size decreased from 10.60 in generation 28 to 8.09 in generation 30 (pairing dates were from 1968/143 to 1968/234), and did not reach the original level for the rest of the generations. The linear regression coefficients for the two periods were:

Generations 1 to 28 β=+.03289±.01681 (P=.06)

Generations 29 to 73 β=-.00862±.00681 (P=.21)

In the LX population, there were several instances that the mean litter size showed large changes over a few generations, but the means stayed mainly below the original values after a sharp decrease which occurred from generations 50 to 51 (pairing date 1973/317). The linear trend over the two periods were:

Generations 1 to 50 β=+.00035±.00681 (P=.96)

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[*] Day one is January first

Table VI.7

Large changes in mean litter size in one generation in the main populations

Pop	Gener.	Change†	P.D.‡	Gener.	Change†	P.D.‡
QL	6-7	-2.02	63/063	14-15	+2.22	65/036
	27-28	+2.16	68/051	40-41	+2.20	71/139
	49-50	-2.72	73/226	62-63	+2.08	76/314
LX	1-2	-2.00	61/353	18-19	-1.59	66/017
	22-23	-1.44	66/354	37-38	-1.48	70/231
	49-50	+1.83	73/226	50-51	-1.47	73/317
NB	4-5	+1.85	62/260	5-6	-2.62	62/337
	19-20	+1.66	66/108	28-29	-2.29	68/143
	38-39	+2.22	70/322	42-43	-1.82	71/321
OC	15-16	+2.00	66/109	20-21	-1.86	67/149
	29-30	+1.05	69/231	51-52	-1.37	75/041
AC	2-3	+1.70	63/065	7-8	-2.08	64/155
	9-10	+1.32	64/317	35-36	-1.30	71/033
	56-57	+1.37	76/118	65-66	+1.13	78/219
CD	16-17	+2.45	66/185	22-23	-1.61	67/311
	25-26	-1.43	68/219	38-39	+2.05	71/306
	48-49	-1.43	74/120	58-59	-1.38	76/307
IC	1-2	-2.23	63/331	12-13	+1.98	65/188
	13-14	-1.74	65/263	18-19	+1.62	66/339
	19-20	-1.79	67/052	61-62	-1.68	77/206
GL	2-3	+1.04	63/154	3-4	-0.86	66/260
	15-16	+1.25	66/201	64-65	-1.00	78/215

† Mean litter size in any generation minus that in the previous generation.

‡ Pairing date of the generation which showed the change.

Generations 51 to 73 $\beta=-.00504\pm.01552$ (P=.75)

Although the trend of litter size over all the generations was significant in these three populations, it remained virtually stable over each period. The CD population also showed several large generation to generation changes in mean litter size. However, after decline from 9.32 in generation 25 to 7.89 in generation 26 (pairing date 1968/219), and another decline from 8.48 in generation 48 to 7.07 in generation 49 (pairing date 1974/120) the means in most of generations stayed below what they were during the preceding period. The significant decline in litter size over all generations in this population was therefore mainly the result of two sharp decreases, with no appreciable trend during each period. The regression coefficients for each of the periods were:

Generations 1 to 25 $\beta=-.00468\pm.02133$ (P=.83)

Generations 26 to 48 $\beta=-.01814\pm.01624$ (P=.28)

Generations 49 to 69 $\beta=-.00582\pm.01618$ (P=.72)

The positive and significant trend of litter size by generations which was observed in the GL population was entirely due to the positive trend from generation one to 16 ($\beta=+.08066\pm.01953$, $P<0.01$), after which litter size showed no trend ($\beta=+.00018\pm.00308$, P=.95). Litter size in the QL, AC and IC populations behaved differently from the others, as litter size showed no trend over all generations. It should be noted that it was possible to choose several periods, each covering at least 10 generations, in which litter size showed large and highly significant positive or negative trends in most of the populations. The QL and AC populations are examples of those having such short-term and temporary trends. Comparison between such short term trends in different populations did not produce a noteworthy result.

In order to further examine the behavior of the litter size variation by generation, the pairing dates of mice in several generations in each population in which the large change (positive or negative) occurred in one generation were studied, and the results are shown in Table VI.7. Fluctuations of mean litter size by generation in the GL and OC populations were neither frequent nor large in magnitude, while in some other populations, such as NB and QL, large changes over one generation were quite frequent. The detailed comparison of the pairing dates of those generations which showed large changes in the mean litter size indicated that in no single mating season did all the populations which were mated at the same time (±2 days) exhibit similar changes. In some cases, 2 out of 4 populations paired on the same day showed large positive or negative changes over one generation, while the other two showed very small changes. For instance, the NB population showed a large negative change from generation 5 to 6 and so did the population IC from generation 1 to 2, both paired within a few days. Similarly, the NB and OC populations showed large positive changes from generation 19 to 20 and

Table VI.8

Regression of mean litter size of the replicates on generation number over the periods in which the trend was linear by population

Pop.	Generation	β±SE	P†	P.D.‡
QL-R	14-54	+.01333±.01044	0.21	1974/309
	55-72	+.00982±.02964	0.75	
LX-R	23-52	+.00351±.02202	0.88	1974/148
	53-72	-.06438±.02833	0.04	
NB-R	18-28	+.10099±.08684	0.27	1968/247
	29-46	+.02307±.02792	0.42	1973/059
	47-71	-.01063±.00862	0.59	
OC-R	10-53	+.01003±.01110	0.37	1975/217
	54-68	+.03793±.04116	0.37	
AC-R	18-46	+.02472±.02174	0.23	1973/310
	47-68	-.00448±.02739	0.87	
CD-R	16-48	-.02449±.01493	0.11	1974/126
	49-68	-.02395±.03090	0.45	
IC-R	18-42	+.00464±.02043	0.82	1972/313
	43-59	-.05706±.05934	0.35	
GL-R	18-53	+.00807±.01333	0.55	1975/328
	54-67	-.12118±.04840	0.03	

† Significance level.

‡ Pairing date of the generation which showed discontinuity or change of trend.

Table VI.9

The large changes in mean litter size in one generation in the replicates

Pop	Gener.	Change†	P.D.‡	Gener.	Change†	P.D.‡
QL-R	14-15	-1.83	65/039	24-25	+3.29	67/142
	32-33	-1.77	69/132	38-39	-1.89	70/313
	55-56	-1.71	75/035	69-70	-1.81	78/220
LX-R	27-28	-1.73	68/041	42-43	+2.88	71/333
	43-44	-3.21	72/060	45-46	+2.11	72/242
	52-53	-1.89	74/148	69-70	-2.20	78/247
NB-R	18-19	-2.16	66/102	19-20	+2.89	66/186
	36-37	-2.07	70/245	37-38	+1.91	70/336
	53-54	-1.74	74/329	56-57	+2.54	75/237
OC-R	23-24	-2.73	68/043	40-41	-2.72	72/129
	41-42	+2.65	72/243	47-48	-2.79	74/035
	48-49	+2.68	74/127	53-54	-2.44	75/217
AC-R	23-24	-2.45	68/044	24-25	+3.14	68/135
	34-35	-2.54	70/317	43-44	-2.33	73/037
	44-45	+2.21	73/128	57-58	+2.14	76/216
CD-R	28-29	-2.76	69/133	29-30	+2.03	69/224
	39-40	+1.90	72/039	48-49	-1.97	74/126
	51-52	-2.75	75/034	52-53	+2.61	75/126
IC-R	20-21	-2.90	67/143	21-22	+2.14	67/227
	48-49	+2.56	74/126	51-52	-4.73	75/034
	52-53	+3.48	75/125	58-59	+2.90	76/306
GL-R	20-21	+2.27	67/247	21-22	-2.00	67/339
	49-50	-2.23	74/329	53-54	-2.44	75/328
	56-57	+1.59	76/236	63-64	-1.74	78/156

† Mean litter size in any generation minus that in the previous generation.

‡ Pairing date of the generation which showed the change.

15 to 16 respectively, both of them mated at 1966/108, while other populations which were mated at the same date did not undergo the same change. There were also cases in which one of the populations which was paired at the same day showed large and positive change with respect to the previous generation, while another exhibited a large and negative change, and still others did not show any appreciable change. Examples are the QL and AC populations in generations 6 to 7 and 2 to 3 respectively (pairing date 1963/064), and the QL and LX both from generation 49 to 50 (pairing date1973/226).

Generation to generation variation in the replicates was more frequent and larger in magnitude than that in the main populations. It was possible to identify several time periods of around 10 generations each in every population during which the linear trend of mean litter size on generation number was positive or negative with a sharp slope. However, the phenomenon of sharp decrease in the mean litter size in some generations which resulted in permanently smaller than the original level of mean litter size was observed in most of the populations. The phenomenon was particularly clear in the QL-R and LX-R populations. The coefficient of linear regression for each period, initially determined by piecewise regression, are shown in Table VI.8. There was no significant trend in litter size over each period except during the later generations in the LX-R and GL-R populations. The pairing date of mice in those generations which resulted in discontinuity of the regression function or change of the trend (Table VI.8) indicated that such changes happened from late 1972 (in IC-R) to late 1975 (in GL-R), but not in the same breeding season in all populations. The generation number and pairing dates in which mean litter size showed a large change in one generation are presented in Table VI.9. There was no mating season in which all the populations that were mated at the same time (±2 days) showed large positive or negative change over their previous values. For example, the QL-R, IC-R and CD-R populations showed large and negative change when mated on 1975/034, while the OC-R and AC-R populations with the same pairing date did not undergo similar changes.

Patterns of fluctuation in litter size:

The runs test was conducted on the deviation of generation means from the regression lines and the results are shown in Table VI.10. The hypothesis which was tested was whether the residuals fluctuated in a random fashion or whether the sequence by which the means fluctuated was a function of values of the previous means. The results indicated that the fluctuations significantly deviated from a random pattern in the GL, OC, LX-R and AC populations, which indicate that the means remained above or below the mean of residuals (zero) more or less frequently than would be expected from a purely stochastic process. the few number of runs, such as in the LX-R population, indicated that the means remained above or below the overall mean for several successive generations.

The time series models which best described the time related patterns of litter size are shown in Table VI.11. There were strong patterns in the fluctuations of litter size from generation to generation in all populations except in the LX, in which the fluctuation was white noise (random error). The pattern of fluctuations were not, however, similar in different populations. The fluctuations in the GL population was best described by a first order nonseasonal autoregressive model, indicating that the mean litter size at any generation was a function of the mean in the previous generation plus a random error. The best time series models for the IC and QL-R populations were first order seasonal autoregressive, indicating that the mean litter size at any generation in IC and QL-R populations was a function of the means at 6 and 2 generations back respectively, but were not related to the means in the previous generations. The best models describing the litter size fluctuations in the QL, AC, AC-R and IC-R populations had a first order nonseasonal autoregressive part and a first order seasonal autoregressive part. These models suggested that mean litter size at any generation was a function of the mean in the previous generation and the mean in *k* generations back and *k*, which is the number of time lags in seasonal part of the model, varied in different populations. It should be noted that the mean litter size in all the above populations, in

Table VI.10

Runs tests for the mean of litter size per generation as deviation from the regression line

POP	No. of runs	Number of cases Less than mean	 More than mean	Z	P
QL	30	38	34	-1.67	.09
QL-R	28	31	28	-.64	.52
LX	37	37	36	-.12	.91
LX-R	17	28	22	-2.51	.01
NB	37	39	34	-.08	.94
NB-R	29	26	28	.28	.77
OC	25	34	35	-2.55	.01
OC-R	29	29	30	-.39	.69
AC	27	32	37	-2.03	.04
AC-R	20	22	29	-1.74	.08
CD	39	36	33	.86	.38
CD-R	29	25	28	.44	.66
IC	32	38	31	-.77	.44
IC-R	24	19	23	.53	.59
GL	23	29	38	-2.73	.00
GL-R	21	24	26	-1.42	.15

which fluctuations were described by autoregressive models, were stationary.

The mean litter size in the GL-R and OC populations were not stationary, and the fluctuations in the series after taking the first difference were best described by a first order nonseasonal moving average model. Such models indicated that the mean litter size at any generation was equal to the mean in the previous generation plus a portion of error term of the previous generation and a new error. The time series models for the OC-R, LX-R, NB, NB-R, CD and CD-R populations had a first order nonseasonal moving average part and a first order seasonal moving average part, and all but the CD-R population were nonstationary. Such models indicated that in these populations, except the CD-R, mean litter size at any generation was equal to what it was in the previous generation plus a portion of the error term in the previous generation, a portion of error term in the *k* generation back, and a new error.

There was no relationship between the genetic heterogeneity of the populations and the type of time series models, i.e. whether the mean at any generation was a function of previous means (autoregressive model) or a function of previous error terms (moving average model). There was not any definite relationship between the type of the model and the environmental conditions under which the populations were kept, as fluctuations in almost half of the populations maintained in each environment were best described by autoregressive and half by moving average models. An interesting observation was the consistency between the type of models (autoregressive or moving average, irrespective of the seasonal patterns) in the main populations and their corresponding replicates. The models in the QL, AC and IC populations and their replicates were autoregressive, while in the NB, OC and CD populations and their replicates were moving average. However, the main populations and their replicates were not consistent with respect to the presence or absence of seasonal patterns or the seasonal time intervals. The fluctuations in the

Table VI.11

Time series models describing the fluctuations of litter size from generation to generation

Pop.	Time series models†	ARIMA‡
QL	$Y_t(1-.174\ B)(1+.344\ B^9)=8.089+\epsilon_t$	$(1,0,0)(1,0,0)^9$
QL-R	$Y_t(1-.289\ B^2)=8.935+\epsilon_t$	$(0,0,0)(1,0,0)^2$
LX	$Y_t=9.396+\epsilon_t$	$(0,0,0)(0,0,0)$
LX-R	$Y_t(1-B)=(1-.674\ B)(1+.261\ B^{14})\epsilon_t$	$(0,1,1)(0,0,1)^{14}$
NB	$Y_t(1-B)=(1-.934\ B)(1-.414\ B^{12})\epsilon_t$	$(0,1,1)(0,0,1)^{12}$
NB-R	$Y_t(1-B)=(1-.970\ B)(1-.469\ B^9)\epsilon_t$	$(0,1,1)(0,0,1)^9$
OC	$Y_t(1-B)=(1-.667\ B)\epsilon_t$	$(0,1,1)(0,0,0)$
OC-R	$Y_t(1-B)=(1-.840\ B)(1+.141\ B^2)\epsilon_t$	$(0,1,1)(0,0,1)^2$
AC	$Y_t(1-.490\ B)(1-.232\ B^7)=4.390+\epsilon_t$	$(1,0,0)(1,0,0)^7$
AC-R	$Y_t(1-.581\ B)(1+.454\ B^{10})=3.596+\epsilon_t$	$(1,0,0)(1,0,0)^{10}$
CD	$Y_t(1-B)=(1-.713\ B)(1-.223\ B^9)\epsilon_t$	$(0,1,1)(0,0,1)^9$
CD-R	$Y_t=8.259+(1+.146\ B)(1+.338\ B^3)\epsilon_t$	$(0,0,1)(0,0,1)^3$
IC	$Y_t(1-.362\ B^6)=8.274+\epsilon_t$	$(0,0,0)(1,0,0)^6$
IC-R	$Y_t(1-.235\ B)(1-.554\ B^4)=6.371+\epsilon_t$	$(1,0,0)(1,0,0)^4$
GL	$Y_t(1-.462\ B)=5.531+\epsilon_t$	$(1,0,0)(0,0,0)$
GL-R	$Y_t(1-B)=(1-.547\ B)\epsilon_t$	$(0,1,1)(0,0,0)$

† B is backward shift operator ($Y_tB=Y_{t-1}$) and ϵ_t is random error.

‡ Autoregressive- integrated- moving average (see Appendix VI.2).

majority of the populations showed seasonal patterns, but the time periods were highly variable across populations. The seasonal time periods in the OC-R and QL-R were 2, and that for the IC-R was 4, showing the possibility of environment related fluctuations.

VI.5. Discussion

Various analyses were performed in this chapter in an attempt to explain the observed patterns of variation and the trends of litter size over generations. The between generations variation, which were highly significant in most of the populations, were the net result of many factors which can be classified into three groups:

i-Continuous and directional forces such as inbreeding and natural selection, which change the genetic structure of a population, and trends in the environmental conditions, both of which would change the phenotypic value of any trait.

ii-Cyclical variations resulting from environmental changes (such as seasonal variations which could have particularly affected the replicates), or due to cyclical changes in the rate of inbreeding as a result of the particular mating system which was followed in this experiment.

iii-Random fluctuation due to temporary environmental factors and sampling variation which could create an erratic pattern of variation in the performance of populations from generation to generation. Such variations are not correlated in different generations and are not expected to produce steady drift.

It would be impossible to accurately separate the above sources of variation with only one replication from each genetic source. Nevertheless, the relatively large number of populations each maintained in two environments would certainly help the interpretation of the results.

The ranges of fluctuations of mean litter size were quite large in most of the populations, particularly in those which were maintained in the uncontrolled environment. There are very few reports which describe specifically the range of fluctuation of litter size in control populations of mice. Examination of the plots of mean litter size by generation in control populations of mice maintained under controlled environmental conditions reported in the literature showed that the ranges of fluctuations were close to the values obtained for the main populations in the present study. For example, the average of mean litter size of 6 control strains of mice fluctuated between approximately 8.5 to 11 over 23 generations (Falconer, 1973). Mean litter size in a population maintained for 24 generation fluctuated between approximately 6 to 9 (Bradford, 1971). The control populations studied by Eklund and Bradford (1977) and Bakker *et al*. (1978) fluctuated between approximately 6 to 9 and 7 to 11 respectively. Data reported by Rahnefeld *et al*. (1966) show that mean litter size in an inbred line of mice changed between 3.6 to 6.7 over 30 generations. Falconer (1960b) reported a small range of generation to generation fluctuations (1.7) for mean litter size (live born) in a control population.

The larger maximum values for mean litter size in the replicates compared with those in the main populations, which were observed in many generations in most of the populations (Appendix VI.1), is an interesting phenomenon. This phenomenon not only increased the range of fluctuations in mean litter size, but also resulted in a larger overall mean for the replicates as compared with the main populations. The higher levels of heterozygosity of the replicates compared with those in the main populations, as discussed in the previous chapter, is probably a reasonable explanation for this phenomenon.

The components of total phenotypic variance explained, at least to some extent, the causes of variation in litter size. The small but significant between generations component of variance in almost all populations is in agreement with the finding of Falconer (1960b) for a control population of mice over 28 generations. The between generations component of variance in the Falconer's study was only 2.5% of the within generations variance, which is reasonably close to the values obtained for the main populations in the present study. The small value of $\sigma^2 b$ in Falconer's experiment surprised him, as he expected larger values due to many possible sources of variation, which he assumed had some effects on litter size in different generations compared with more uniform environmental condition for the contemporaneous individuals. The result of the present study showed that the effects of factors which influence litter size in different generations of a population maintained in a controlled environment might in fact be relatively small, as σ^2b's of the replicates in the present experiment were larger than those of their corresponding main populations. Furthermore, the contemporaneous individuals within each generation were possibly subjected to much larger environmental variations than what Falconer had assumed. The ranges of litter size variability in population- generation subclasses rarely were below 10. This large within generation variability, which seems to be characteristic of litter size, could have been due to the complex genetic and environmental factors controlling litter size. Death losses at various stages of embryonic development due to many genetic and environmental factors, as described in the previous chapter, would increase the variance of litter size in each generation.

Falconer (1960b) reported that approximately 50% of the variability of mean litter size between generations was attributable to sampling and 50% to real difference between generations. These estimates are in the lower boundary of the corresponding estimates for the main populations in the present study (Col. 5, Table VI.3). The agreement between the within generation variance observed in the present study, and the expected genetic heterogeneity of the populations was expected on the basis of genetic theory.

Trends in litter size:

In order to accurately separate the effects of inbreeding from environmental trend, several contemporary groups with the same genetic composition are required. Different lines derived from one base population commonly show various responses to inbreeding (Falconer, 1960b; 1973; Eisen and Hanrahan, 1974), and the average inbreeding depression of several lines from the same origin would be required to obtain an accurate estimate of inbreeding depression. There were several obstacles that stood in the way of drawing firm conclusions from any observed trend or pattern in changes of litter size over generations or as a result of inbreeding in this study. One problem was that the inbreeding coefficient and generation number were highly confounded in this study (as in other studies of the same nature). In some studies, traits have been regressed on either generation number, assuming small inbreeding effect (King *et al.*, 1963; Merritt, 1968), or on inbreeding coefficient, assuming no trend in environmental conditions (Beilharz, 1982), depending on the objectives of the investigator. Ibe *et al.*(1983) computed regression of mean of several traits (as deviation from a control line) in poultry on generation number and inbreeding coefficient separately, and found similar results in both analyses, as might be expected.

Pooled regression is one method of estimating inbreeding depression, if within generation variances and regressions are homogeneous. However, the narrow range of inbreeding coefficients among families within generations due to the nature of the mating system, and the heterogeneity of variances in some populations reduced the reliability of the pooled estimates as a measure of inbreeding depression. In fact, if litter size had declined according to the rates estimated from the pooled regression coefficients, then the total decline due to inbreeding attained through the course of the study would have been much larger than what was actually observed. Various experiments with mice have shown that fitness traits exhibit inbreeding depression under rapid inbreeding. The estimates of inbreeding depression in litter size per one percent increase in inbreeding coefficient are reported to be -.056 (Bowman and Falconer, 1960) and -.049 (Falconer, 1960b). Slow rate of inbreeding, on the other hand, may not have the same effect as rapid inbreeding. Controversial results have been reported on the effects of slow inbreeding on litter size in mice. Eisen (1978) reported the regression of litter size on individual inbreeding coefficient, pooled over 12 generations, to be insignificant ($b=0.053\pm0.048$). Inbreeding depression of litter size in a control population of mice over 25 generation was not significant ($b=-.0275$) as reported by Beilharz (1982). On the contrary, Falconer (1973) observed a steady decline in the average litter size in 6 control strains of mice (Q-strain) each maintained for 23 generations from 10.5 to 9.0, with final coefficient of inbreeding of about 30%. He attributed the decline to inbreeding depression (corresponding to 0.05 young per 1% inbreeding).

The reason for the different effects of rapid and slow inbreeding on rate of decrease in performance is mainly the counteracting effect of natural selection which would have a greater opportunity to operate when rise in the inbreeding coefficient is gradual, which also implies that population size is large. The original plan in this study was to choose one male and one female from each litter, which would have resulted in virtually no selection for litter size or maternal effect. In practice, however, infertility and death losses resulted in differential contribution of various families to the next generation, which could have resulted in non-zero selection differential. A consequence of the adverse effect of inbreeding on a trait such as litter size is that, individuals selected for breeding from a given generation are likely to be in the lower range of inbreeding coefficient for that generation. The survivors are therefore a selected group to which the theoretical expectation no longer applies, i.e. the inbreeding coefficient does not reflect the probability of genes being identical by descent. Thus, the precise measurement of the average effect of inbreeding on a trait over a long period will lose its accuracy, and the estimate of inbreeding depression based on the pooled regression may not measure the actual reduction in litter size over a large number of generations.

Another problem in accurate estimation of the inbreeding depression was the maternal effect on litter size and separation of the inbreeding effects of dam and progeny on this trait. The maternal traits are among the most sensitive characters to inbreeding depression, and the effect of inbreeding on litter size, a trait which is highly influenced by maternal effect, is therefore twofold. Such complications have made it very difficult, if not impossible, to single out with any degree of accuracy, the relative importance of different sources on the variation of litter size over generations. The inbreeding coefficient of the progeny is usually one step ahead of that of the mother, but in the present study, due to the nature of the particular mating system which resulted in fluctuation of inbreeding coefficients over generations, this relationship did not hold for all the generations. Furthermore, due to the slow rate of inbreeding per generation, the difference between the inbreeding coefficients of mother and progeny was not large enough to be detectable, as the pooled regressions of litter size on the inbreeding coefficients of progeny and dam were close to each other. The effect of inbreeding, as measured here is therefore, the combined effects of inbreeding on the progeny and the dam. The above mentioned considerations might suggest that the behavior of the populations with respect to generation number should perhaps receive much greater emphasis than inbreeding depression.

Two notable phenomena were detected in studying the trends of litter size over generations. First, there was no steady trend in mean litter size by generations over the whole course of the study in many of the populations, and the observed trends rather revealed some forms of discontinuity in the regression lines which permanently changed the mean litter size, or showed a change in the trend at some generations. The second phenomenon was the presence of several short-term trends (about 10 consecutive generations each) with significantly positive or negative slope within each of the populations. These observations support the hypothesis that, inbreeding had not been the only factor which caused the observed negative trends in litter size, as it was unlikely that inbreeding alone could have caused such changes.

The reported trends in litter size over generation in control populations of mice are variable in direction and magnitude, but usually linear. Dalton and Bywater (1963) reported stable litter size at weaning over 17 generations in two control populations fed normal (b=0.03±0.03) or diluted diets (b=-.05±0.03). Eisen *et al*. (1970) did not observe any significant trend in litter size for two replicate control populations of mice (b=-.03±0.04 and b=0.01±0.06) over 10 generations. Falconer (1971) for 30 generations (regression coefficient was not reported) and Eisen (1978) for 12 generations (b=-.05±0.04) did not find any significant trend for litter size in control populations of mice by generation, but Eisen and Hanrahan (1974) and Bakker *et al.* (1978) observed significant decrease in this trait by generation (b=-.039±0.017 and b=-0.03±0.02 respectively). On the contrary, Eklund and Bradford (1977) detected a significantly positive trend (b=+.021±0.007) in litter size over 45 generations. The linear regressions of litter size by generations, pooled over several replicates, in control populations of mice maintained for 15 generations (Eisen and Hanrahan, 1974) were -.067 ($P<.05$), -.092, +.051, -.104 ($P<.05$), +.014 and -.181 ($P<.05$) for population sizes of 16, 8, 8, 4, 2 and one pairs respectively. No adjustments have been made for the inbreeding effect in any of these cases (as it was not practically possible to do so). The linear regression coefficients of litter size on generation number obtained in the present study were within the wide range of the reported estimates. The main conclusion which can be made from the present study and the reported values in the literature is that, the long-term trend of litter size in a control population is not predictable, even if the environmental conditions are held as constant as possible and population size is large. The conflicting conclusions made by Falconer(1960b) and Eisen and Hanrahan (1974) regarding the long-term trends of litter size clearly indicate that the subject is still controversial and unresolved.

The large positive or negative trends over several consecutive generations is an important observation particularly where control populations are used for removing environmental time trends in short-term selection experiments. In a control line of mice, Joakimsen and Baker (1977) observed no trend in mean litter size by generation during the first 7 generations (b=0.07±0.06), and a negative and insignificant trend (-.19±0.10) was detected from generations 8 to 15, resulting in an overall significant trend (-.10±0.03). At least three periods with large negative or positive trends could be detected in the plot of litter size by generations reported by Eisen and Hanrahan (1974). Inspection of the plot of mean litter size in a control population of mice maintained for 24 generations reported by Bradford (1971) also indicated different short-term time trends, a steady decline from generations one to 8 followed by a positive trend from generations 8 to 22. The results of the present study showed that such trends are not entirely caused by environmental factors, and therefore two or more lines, control or selected, may not necessarily undergo similar trends. Consequently, any conclusion based on a single control population might be misleading.

There was no clear correspondence between the expected genetic heterogeneity of the populations and the magnitude or direction of trends of litter size by inbreeding or generation number. More surprisingly, the CD and AC populations, which originally had 50% of their genes in common, behaved quite differently. This differential response is difficult to interpret, but it could be postulated that genetic differences between these two populations could have been larger than expected, possibly due to the accumulation of different mutant genes in each population and genetic drift.

The fact that the contemporaneous populations did not share similar changes in litter size indicated that the observed variations could not be fully accounted for by the environmental factors. The repeatabilities were calculated for the generation means of the populations which were mated at the same time or within each breeding season to test whether the differences in environmental factors affecting each generation had any consistent effect on all the populations. The generation numbers were modified so that all the populations which were paired at the same season had identical numbers. The between generation ($\sigma^2 bg$) and between populations within generation ($\sigma^2 wg$) variance components were computed, and repeatabilities were calculated as $\rho=\sigma^2 bg/(\sigma^2 bg+\sigma^2 wg)$. The much larger between populations within generation variances compared with the between generation variances in all the cases, which resulted in very low repeatability estimates (Table VI.12), confirmed the previous conclusion that the environmental factors did not uniformly affect all the contemporary groups as far as litter size was concerned.

When population size is large, as was the case in the present study, the drift variance is small and differential

Table VI.12

The between generations (σ^2bg) and between populations within generation (σ^2wg) components of variance and the estimates of repeatability (ρ) of mean litter size

Populations†	σ^2wg	σ^2bg‡	ρ
QL, LX, NB	.6929	-.0101	.000
AC, CD, IC	.6224	-.0398	.000
OC, GL	.6995	-.1967	.000
Main populations combined	1.1910	-.0651	.000
QL-R, LX-R, NB-R, OC-R, GL-R	1.5020	.1450	.088
AC-R, CD-R, IC-R	.7224	.4063	.360
Replicate populations combined	1.5168	.2199	.127

†The pairing dates of all the populations in each group were within a few days in each season except when all the populations were combined.

‡Negative variance components were assumed to be an estimate of zero.

trends in different populations over time are not likely to be due to drift (Eisen and Hanrahan, 1974). Falconer (1973) reported that inbreeding depressions were different in 6 control populations of mice maintained for 23 generations, and one of the populations did not show any inbreeding depression. He claimed that the upward drift occurred at the same rate as inbreeding depression in the line whose performance did not decline. It is difficult to interpret the observed patterns of trend of litter size by generations in the present study with respect to drift alone.

The results may suggest that long-term changes in litter size are highly complicated and cannot be fully explained by either drift, inbreeding depression or environmental factors. It seems reasonable to postulate that some genetic changes in the population, due to inbreeding, genetic drift, or natural selection, would create a genetic structure which, under some particular environmental conditions, may lead to a major and permanent change in litter size

Patterns of fluctuations of mean litter size:

The generation to generation fluctuations of phenotypic traits which are normally large in magnitude, as were discussed earlier, have been considered in the literature as random variation. There are, however, many different types of variation which cannot be explained by regression equations, although they may possess a definable pattern. The sine waves and seasonal variations are the examples. The runs test indicated that the residuals were random in most of the populations, while significant correlations among residuals were shown by the time series analysis. In runs tests, a small positive deviation from the overall mean will count as much as a large positive deviation, thus runs test, even though very simple to conduct, is not a very powerful method to detect the nonrandomness of a series of time-related observations. Time series analysis, on the other hand, is a powerful method for detecting and quantifying the time-related patterns.

Regression analysis and time series analysis are complementary when the observations are recorded in specific time intervals. The former assumes a cause and effect relationship between two variables, while the latter treats the system as a black box and makes no attempt to discover the factors affecting the behavior of the system. There are two major reasons for trying to treat a system as a black box. First, the causal relationship between variables may not be truly understood, or it may be extremely difficult to measure the relationships assumed to govern its behavior. Second, the main concern may be only to discover *what is happening* rather than *why it is happening*. In time series analysis it is not the choice of independent variables, but the observed values that are used to explain their own behavior. To the best of the author's knowledge, no attempt has so far been made to use time series analysis, or any other method, to explain such fluctuations. Dalton and Bywater (1963) mentioned the presence of rhythmic seasonal variation in the generation means of litter size based on visual inspection of the data. Beilharz (1982) claimed the existence of a rhythmic variation in mean litter size in a control population of mice, and the variations followed similar changes in the inbreeding coefficients caused by a particular cyclical mating system. Eisen and Hanrahan (1974) observed a cyclical variation in litter size over 26 generations in a control stock population, and found a polynomial of degree four as the best equation fitted to the data. Their equation, even though it fitted their data quite well (R^2=.51) did not seem to be very appropriate because deletion of observations in the last few generations resulted in a completely different equation (possibly a third degree polynomial), and extrapolation of the curve resulted in unacceptably large values (>20) within a few extra generations. They stated that the mean litter size in the last few generations, which were not used to fit the polynomial, were in the range of the original values. The information given in their paper clearly suggested the presence of a cyclical pattern, and strongly ruled out the validity of a polynomial regression as an acceptable method for explaining the behavior of the data. The limited number of generations recorded in most experiments have made it impossible to conduct a meaningful test for identification of generation to generation fluctuations, and in those cases where sufficient numbers of generations were recorded, no attempt was made to analyze the results properly.

Using time series analysis is justifiable on the ground that the residuals of the regression analysis were correlated. This is a violation of one of the most important assumptions in regression analysis. Such violation would reduce the validity of the results of regression analysis. Furthermore, the large correlation coefficient between generation number and inbreeding coefficient, and the controversy about whether inbreeding or environmental time-trends caused the decline of litter size, made it worthwhile to use the time series analysis, hoping to gain a more accurate picture of the behavior of litter size variation.

The differential patterns of fluctuations in litter size over generations, as detected by the time series analysis, made it difficult to make a general conclusion about the behavior of the populations or usefulness of the time series methodology for analysis of biological systems. The consistency in the main populations and their replicates in most cases with respect to the type of models (autoregressive or moving average) suggested that the pattern of fluctuations in the mean litter size from generation to generation probably had a genetic basis. The lack of any relationship between the origin of the population and the type of time series model may suggest that the fluctuation was independent of genetic heterogeneity. The time period of the seasonal patterns is the key for interpretation of the fluctuation observed in mean litter size. Inbreeding coefficients in the main and replicate populations had a sharp jump after each 12 (or 24) and 7 (or 14) generations respectively. Therefore, if litter size had responded negatively to such sudden increases, as reported by Beilharz (1982), seasonal time lags of these magnitudes should have been detected. Such seasonally related patterns were observed only in the NB population (lag 12) and the LX-R population (lag 14). The inconsistency in the seasonal time periods in the main populations suggested that the observed fluctuation more likely had a non-environmental origin, but it is difficult to interpret them with regards to the genetic constitution of the populations. Since the effective population sizes were fairly large in this experiment, it is expected that the drift variances would generally be small, and should not have resulted in the observed generation to generation fluctuation. Seasonal variation in the environmental conditions was expected to influence the mean litter size in the replicates. The seasonal time periods of 2 and 4 in the OC-R, QL-R and IC-R populations showed that the time series analysis was successful in detecting such seasonal patterns whenever those existed.

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APPENDICES

Appendix II.1. Genetic heterogeneity of the foundation stocks

Information about the genetic heterogeneity of the foundation stocks would be helpful for the interpretation of the results. History of the mice and the method by which the stocks were formed provide some information about their genetic heterogeneity. A hypothetical random-bred population of laboratory mice could be considered as a reference point to which all the stocks will be compared.

As the history of the inbred lines indicate, they can be regarded as pure-lines (F=1) with no relation to each other. It may be assumed that all the gametes produced by any one of the pure-lines are genetically identical, but the gametes of one line do not have any relationship with those of the other lines. Based on this assumption, each pure-line can be considered as one gamete selected from a random-bred population. It has been shown both theoretically (Haldane, 1936) and experimentally (Gruneberg, 1954) that some heterozygous loci could be found in pure lines, mainly due to linkage, new mutations and overdominance. The level of heterozygosity is, however, very small and cannot be quantified. The effects of long term inbreeding on the genetic constitution of each line is a matter of speculation.

The highly inbred strains of mice commonly available in mouse laboratories represent a relatively few chance survivors from hundreds of attempts to establish inbred strains in the past. What was special about those lines which enabled them to stand very high levels of inbreeding is not clearly understood. The very high level of homozygosity of pure-lines implies that they cannot carry lethal or seriously deleterious genes disregarding new mutations. Likewise crosses between inbred lines do not carry such genes. An outbred population can carry many genes of this nature in heterozygous state. Falconer (1953) argued that selection for fitness, which inevitably takes place during the formation of the inbred lines, should be expected to have a different effect for fitness in a random-breeding population, since it acts chiefly on homozygous loci. Thus some genes which affect both size and fitness would be expected to be more frequent and others less frequent in a population of inbred lines compared to a random-bred population. Such pure-lines are, therefore, a very unique and particular gamete of a random-bred population, and all the results of experiments involving crosses between pure-lines are undertaken at a considerable loss of generality.

Falconer (1953) believed that by crossing unrelated inbred lines, probably more genetic variance is introduced than is commonly found in single populations of laboratory mice breeding at random. Regardless of what has happened to the genetic make up of pure-lines throughout the course of inbreeding, when a few lines are being used, they represent only a few gametes from a hypothetical outbred population and therefore chance can play a decisive part when a segregating population is synthesized from inbred strains. Therefore, estimates of the population parameters are subject to large sampling errors if they are going to be related to the hypothetical base population from which they were supposedly derived.

The assumption of similarity of all the gametes produced by an inbred line, and the absence of any relationship between any two lines, implies that all the progeny resulting from cross between any two pure lines are genetically identical and could be considered as a replicate of one single individual taken from a random-bred population. That individual has been the result of union of two unrelated gametes, thus its inbreeding coefficient is zero. Stock populations AC and CD are of this type. Sex linked genes in female progeny of reciprocal cross between any two lines are genetically the same, while males may carry different alleles. Generation one, with inbreeding coefficient of 50%, is therefore, genetically equivalent to the product of self-fertilization of an individual. Half of the genes in the progeny of any two crosses with one pure line as their common parent are similar. The relationship between populations AC and CD is of this nature.

Two groups of F1's from two-way crosses without any inbred line as their common parent are genetically the same as two unrelated individuals of a random-bred population. All progeny resulting from matings between two such groups of F1's would genetically be equivalent to a family of full sibs whose parents were taken from a hypothetical random-bred population, thus their inbreeding coefficient would be zero. Population IC was formed in this way. Generation one of this population was therefore genetically equivalent to the product of full-sib mating, and consequently 25% inbred. Original gene frequencies at most of the segregating loci of 2-way and 4-way crosses between inbred lines must have been near 0.25 and 0.5 respectively.

It is difficult to rank the four non-inbred populations from Edinbugh as far as their genetic heterogeneity is concerned. It seems that the Q-strain was the most heterogenous of the four population. This strain could be considered as a sample of a random-bred population of laboratory mice, despite the contribution of the JU inbred line (which was one of its four grand parental lines) which perhaps restricted the range of possible gene frequencies. The OC was possibly the most heterogeneous population, because it was constructed from crosses between four non-inbred populations. The population GL could also be considered very heterogeneous, although half of its genes came from a genetically narrow source (IC).

It appears that there is no relationship between Edinburgh strains and the inbred lines from Maine. The contribution of the C57-BL, which was related to C57-BR/cd, in JH and Q-strains cannot be a matter of concern since it had happened some 30 generations before they were used in this experiment. The the JH and Q-strains were genetically related to each other, but their relationship cannot be quantified.

Appendix III.1. Derivation of the recurrence relationships

Suppose N individuals are assigned into $n=N/2$ cages in each generation and cyclical mating system is followed. Let the cages be designated as A, B, C, . .etc., and individuals be identified by the name of the cage in which they were born. Assume that one male and one female are selected from each cage in each generation (variance of family size is zero) and male progeny retained in the same cage in which they were born, that is, for example, male in cage A is called A in all generations. Females which mated with male A in generations 1, 2, 3, . . were born in cages B, C, D, . . respectively.

A-Homozygosity of an individual:

Applying the equation (1)[a] to the genealogical relationships, and denoting generations by subscripts and female individuals by " ' ", gives the following results:

Generation 1: $f_1(A) = \Phi_0(A,B')$

Generation 2: $f_2(A) = \Phi_1(A,C')$

Generation 3: $f_3(A) = \Phi_2(A,D')$

Generation 4: $f_4(A) = \Phi_3(A,E')$

Generation 5: $f_5(A) = \Phi_4(A,F')$

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[a] Equation number presented in chapter III

etc,. (A3.1.1)

These equations indicate that $f(A)$ at generations 1, 2, 3, . . . t', are a function of the coefficient of identity between father of A at generations 0, 1, 2, . . .t'-1, and a female from k=1, 2, 3, . . . m cages apart. The relationships (A3.1.1) were expressed with respect to the number of steps between cages (k), instead of cage identification and the results for the odd and even n's are shown in Appendix Tables 1 and 2 respectively.

B-*Coefficient of identity of individuals born in the same cage*:

Applying equation (3) to the genealogical relationships gives the coefficient of identity of any two full-sibs A and A':

$$\text{Gen. 1: } \Phi_1(A,A')=(1/2)\{(1/2)[1+f_0]+\Phi_0(A,B')\}$$

$$\text{Gen. 2: } \Phi_2(A,A')=(1/2)\{(1/2)[1+f_1]+\Phi_1(A,C')\}$$

$$\text{Gen. 3: } \Phi_3(A,A')=(1/2)\{(1/2)[1+f_2]+\Phi_2(A,D')\}$$

$$\text{Gen. 4: } \Phi_4(A,A')=(1/2)\{(1/2)[1+f_3]+\Phi_3(A,E')\}$$

$$\text{Gen. 5: } \Phi_5(A,A')=(1/2)\{(1/2)[1+f_4]+\Phi_4(A,F')\}$$

etc., (A3.1.2)

These relationships indicate that the coefficients of identity of full-sibs at generations 1, 2, 3, . . t', are a function of inbreeding coefficients of their parents, and the coefficients of identity between their father and a female which was born in k=1, 2, 3, . . m cages apart in generations 0, 1, 2, . . t'-1. The relationships (A3.1.2) are written with respect to the distance between the cages (k), and the results are depicted in Appendix Tables 3 and 4 for the odd and even n's respectively.

C-Coefficient of identity between individuals born in different cages:

The equation (4) for those individuals born in two adjacent cages (one step apart) leads to the following recurrence equations connecting different generations:

Generation 1:

$\Phi_1(A,B')=(1/4)[\Phi_0(A,B)+\Phi_0(A,C')+\Phi_0(B',C')+\Phi_0(B,B')]$

Generation 2:

$\Phi_2(A,B')=(1/4)[\Phi_1(A,B)+\Phi_1(A,D')+\Phi_1(C',D')+\Phi_1(B,C')]$

Generation 3:

$\Phi_3(A,B')=(1/4)[\Phi_2(A,B)+\Phi_2(A,E')+\Phi_2(D',E')+\Phi_2(B,D')]$

Generation 4:

$\Phi_4(A,B')=(1/4)[\Phi_3(A,B)+\Phi_3(A,F')+\Phi_3(E',F')+\Phi_3(B,E')]$

Generation 5:

$\Phi_5(A,B')=(1/4)[\Phi_4(A,B)+\Phi_4(A,G')+\Phi_4(F,G')+\Phi_4(B,F')]$

etc. (A3.1.3)

Equations (A3.1.3) are written with respect to the distance between cages, and are shown in Appendix Tables 5 and 6 for odd and even values of n respectively.

The equation (4) was used for individuals born in cages with one cage between them (two steps apart). Such individuals are for example, those which were born in cage C with those in cages A and E, those in cage D with those in cages B and F, etc. The coefficients of identity of some individuals are as follows:

Generation 1:

$$\Phi_1(A,C')=(1/4)[\Phi_0(A,C)+\Phi_0(A,D')+\Phi_0(B',D')+\Phi_0(C,B')]$$

Generation 2:

$$\Phi_2(A,C')=(1/4)[\Phi_1(A,C)+\Phi_1(A,E')+\Phi_1(C',E')+\Phi_1(C,C')]$$

Generation 3:

$$\Phi_3(A,C')=(1/4)[\Phi_2(A,C)+\Phi_2(A,F')+\Phi_2(D',F')+\Phi_2(C,D')]$$

Generation 4:

$$\Phi_4(A,C')=(1/4)[\Phi_3(A,C)+\Phi_3(A,G')+\Phi_3(E',G')+\Phi_3(C,E')]$$

Generation 5:

$$\Phi_5(A,C')=(1/4)[\Phi_4(A,C)+\Phi_4(A,H')+\Phi_4(F,'H')+\Phi_4(C,F')]$$

etc. (A3.1.4)

These equations are written with respect to the distance between cages,and are depicted in Appendix Tables 7 and 8 for the odd and even values of n respectively.

Appendix Table 1

Recurrence equations for homozygosity of individuals in successive generations when n is odd

t	c	t'	i	Equation
1	1	1	1	$f_1 (A)=\Phi_0$ (1)
2	1	2	2	$f_2 (A)=\Phi_1$ (2)
3	1	3	3	$f_3 (A)=\Phi_2$ (3)
.	.	.	.	. . . .
.	.	.	.	. . . .
m-1	1	m-1	m-1	$f_{m-1}(A)=\Phi_{m-2}$(m-1)
m	1	m	m	$f_m (A)=\Phi_{m-1}$(m)
m+1	1	m+1	m	$f_{m+1}(A)=\Phi_m$ (m)
m+2	1	m+2	m-1	$f_{m+2}(A)=\Phi_{m+1}$(m-1)
.	.	.	.	. . . .
.	.	.	.	. . . .
n-3	1	n-3	3	$f_{n-3}(A)=\Phi_{n-4}$(3)
n-2	1	n-2	2	$f_{n-2}(A)=\Phi_{n-3}$(2)
n-1	1	n-1	1	$f_{n-1}(A)=\Phi_{n-2}$(1)
n	2	1	1	$f_n (A)=\Phi_{n-1}$(1)
n+1	2	2	2	$f_{n+1}(A)=\Phi_n$ (2)
n+2	2	3	3	$f_{n+2}(A)=\Phi_{n+1}$(3)
.	.	.	.	. . . .
.	.	.	.	. . . .

t: Generation number
c: Cyle
t': Generation within cycle
i: Type of equations
Integer number in parenthesis referring to the number of steps between cages

Appendix Table 2

Recurrence equations for homozygosity of individuals in successive generations when n is even

t	c	t'	i	Equation
1	1	1	1	$f_1 (A)=\Phi_0$ (1)
2	1	2	2	$f_2 (A)=\Phi_1$ (2)
3	1	3	3	$f_3 (A)=\Phi_2$ (3)
.	.	.	.	. . . .
.	.	.	.	. . . .
m-1	1	m-1	m-1	$f_{m-1} (A)=\Phi_{m-2}$ (m-1)
m	1	m	m	$f_m (A)=\Phi_{m-1}$ (m)
m+1	1	m+1	m-1	$f_{m+1} (A)=\Phi_m$ (m-1)
.	.	.	.	. . . .
.	.	.	.	. . . .
n-3	1	n-3	3	$f_{n-3} (A)=\Phi_{n-4}$ (3)
n-2	1	n-2	2	$f_{n-2} (A)=\Phi_{n-3}$ (2)
n-1	1	n-1	1	$f_{n-1} (A)=\Phi_{n-2}$ (1)
n	2	1	1	$f_n (A)=\Phi_{n-1}$ (1)
n+1	2	2	2	$f_{n+1} (A)=\Phi_n$ (2)
n+2	2	3	3	$f_{n+2} (A)=\Phi_{n+1}$ (3)
.	.	.	.	. . . .
.	.	.	.	. . . .

For the description of the symbols see Appendix Table 1.

Appendix Table 3

Recurrence equations for coefficient of identity of full-sibs in successive generations when n is odd

t	c	t'	i	Equation
1	1	1	1	$\Phi_1(0)=(1/2)\{(1/2)[1+f_0]+\Phi_0(1)\}$
2	1	2	2	$\Phi_2(0)=(1/2)\{(1/2)[1+f_1]+\Phi_1(2)\}$
3	1	3	3	$\Phi_3(0)=(1/2)\{(1/2)[1+f_2]+\Phi_2(3)\}$
.	.	.	.	. . . .
.	.	.	.	. . . .
m-1	1	m-1	m-1	$\Phi_{m-1}(0)=(1/2)\{(1/2)[1+f_{m-2}]+\Phi_{m-2}(m-1)\}$
m	1	m	m	$\Phi_m(0)=(1/2)\{(1/2)[1+f_{m-1}]+\Phi_{m-1}(m)\}$
m+1	1	m+1	m	$\Phi_{m+1}(0)=(1/2)\{(1/2)[1+f_m]+\Phi_m(m)\}$
m+2	1	m+2	m-1	$\Phi_{m+2}(0)=(1/2)\{(1/2)[1+f_{m+1}]+\Phi_{m+1}(m-1)\}$
.	.	.	.	. . . .
.	.	.	.	. . . .
n-3	1	n-3	3	$\Phi_{n-3}(0)=(1/2)\{(1/2)[1+f_{n-4}]+\Phi_{n-4}(3)\}$
n-2	1	n-2	2	$\Phi_{n-2}(0)=(1/2)\{(1/2)[1+f_{n-3}]+\Phi_{n-3}(2)\}$
n-1	1	n-1	1	$\Phi_{n-1}(0)=(1/2)\{(1/2)[1+f_{n-2}]+\Phi_{n-2}(1)\}$
n	2	1	1	$\Phi_n(0)=(1/2)\{(1/2)[1+f_{n-1}]+\Phi_{n-1}(1)\}$
n+1	2	2	2	$\Phi_{n+1}(0)=(1/2)\{(1/2)[1+f_n]+\Phi_n(2)\}$
n+2	2	3	3	$\Phi_{n+2}(0)=(1/2)\{(1/2)[1+f_{n+1}]+\Phi_{n+1}(3)\}$
.	.	.	.	. . . .
.	.	.	.	. . . .

For the description of the symbols see Appendix Table 1.

Appendix Table 4

Recurrence equations for coefficient of identity of full-sibs in successive generations when n is even

t	c	t'	i	Equation
1	1	1	1	$\Phi_1(0)=(1/2)\{(1/2)[1+f_0]+\Phi_0(1)\}$
2	1	2	2	$\Phi_2(0)=(1/2)\{(1/2)[1+f_1]+\Phi_1(2)\}$
3	1	3	3	$\Phi_3(0)=(1/2)\{(1/2)[1+f_2]+\Phi_2(3)\}$
.	.	.	.	. . . .
.	.	.	.	. . . .
m-1	1	m-1	m-1	$\Phi_{m-1}(0)=(1/2)\{(1/2)[1+f_{m-2}]+\Phi_{m-2}(m-1)\}$
m	1	m	m	$\Phi_m(0)=(1/2)\{(1/2)[1+f_{m-1}]+\Phi_{m-1}(m)\}$
m+1	1	m+1	m-1	$\Phi_{m+1}(0)=(1/2)\{(1/2)[1+f_m]+\Phi_m(m-1)\}$
.	.	.	.	. . . .
.	.	.	.	. . . .
n-3	1	n-3	3	$\Phi_{n-3}(0)=(1/2)\{(1/2)[1+f_{n-4}]+\Phi_{n-4}(3)\}$
n-2	1	n-2	2	$\Phi_{n-2}(0)=(1/2)\{(1/2)[1+f_{n-3}]+\Phi_{n-3}(2)\}$
n-1	1	n-1	1	$\Phi_{n-1}(0)=(1/2)\{(1/2)[1+f_{n-2}]+\Phi_{n-2}(1)\}$
n	2	1	1	$\Phi_n(0)=(1/2)\{(1/2)[1+f_{n-1}]+\Phi_{n-1}(1)\}$
n+1	2	2	2	$\Phi_{n+1}(0)=(1/2)\{(1/2)[1+f_n]+\Phi_n(2)\}$
n+2	2	3	3	$\Phi_{n+2}(0)=(1/2)\{(1/2)[1+f_{n+1}]+\Phi_{n+1}(3)\}$
.	.	.	.	. . . .
.	.	.	.	. . . .

For the description of the symbols see Appendix Table 1.

Appendix Table 5

Recurrence equations for coefficient of identity of individuals born in adjacent cages in successive generations when n is odd

t	c	t'	i	Equation
1	1	1	1	$\Phi_1(1)=(1/4)[\Phi_0(0)+2\Phi_0(1)+\Phi_0(2)]$
2	1	2	2	$\Phi_2(1)=(1/4)[\Phi_1(1)+2\Phi_1(1)+\Phi_1(3)]$
3	1	3	3	$\Phi_3(1)=(1/4)[\Phi_2(2)+2\Phi_2(1)+\Phi_2(4)]$
.	.	.	.	. . . .
.	.	.	.	. . . .
m-1	1	m-1	m-1	$\Phi_{m-1}(1)=(1/4)[\Phi_{m-2}(m-2)+2\Phi_{m-2}(1)+\Phi_{m-2}(m)]$
m	1	m	m	$\Phi_m(1)=(1/4)[\Phi_{m-1}(m-1)+2\Phi_{m-1}(1)+\Phi_{m-1}(m+1)]$
m+1	1	m+1	m	$\Phi_{m+1}(1)=(1/4)[\Phi_m(m-1)+2\Phi_m(1)+\Phi_m(m+1)]$
m+2	1	m+2	m-1	$\Phi_{m+2}(1)=(1/4)[\Phi_{m+1}(m-2)+2\Phi_{m+1}(1)+\Phi_{m+1}(m)]$
.	.	.	.	. . . .
.	.	.	.	. . . .
n-3	1	n-3	3	$\Phi_{n-3}(1)=(1/4)[\Phi_{n-4}(2)+2\Phi_{n-4}(1)+\Phi_{n-4}(4)]$
n-2	1	n-2	2	$\Phi_{n-2}(1)=(1/4)[\Phi_{n-3}(1)+2\Phi_{n-3}(1)+\Phi_{n-3}(3)]$
n-1	1	n-1	1	$\Phi_{n-1}(1)=(1/4)[\Phi_{n-2}(0)+2\Phi_{n-2}(1)+\Phi_{n-2}(2)]$
n	2	1	1	$\Phi_n(1)=(1/4)[\Phi_{n-1}(0)+2\Phi_{n-1}(1)+\Phi_{n-1}(2)]$
n+1	2	2	2	$\Phi_{n+1}(1)=(1/4)[\Phi_n(1)+2\Phi_n(1)+\Phi_n(3)]$
n+2	2	3	3	$\Phi_{n+2}(1)=(1/4)[\Phi_{n+1}(2)+2\Phi_{n+1}(1)+\Phi_{n+1}(4)]$
.	.	.	.	. . . .
.	.	.	.	. . . .

For the description of the symbols see Appendix Table 1.

Appendix Table 6

Recurrence equations for coefficient of identity of individuals born in adjacent cages in successive generations when n is even

t	c	t'	i	Equation
1	1	1	1	$\Phi_1(1)=(1/4)[\Phi_0(0)+2\Phi_0(1)+\Phi_0(2)]$
2	1	2	2	$\Phi_2(1)=(1/4)[\Phi_1(1)+2\Phi_1(1)+\Phi_1(3)]$
3	1	3	3	$\Phi_3(1)=(1/4)[\Phi_2(2)+2\Phi_2(1)+\Phi_2(4)]$
.	.	.	.	. . . .
.	.	.	.	. . . .
m-1	1	m-1	m-1	$\Phi_{m-1}(1)=(1/4)[\Phi_{m-2}(m-2)+2\Phi_{m-2}(1)+\Phi_{m-2}(m)]$
m	1	m	m	$\Phi_m(1)=(1/4)[\Phi_{m-1}(m-1)+2\Phi_{m-1}(1)+\Phi_{m-1}(m+1)]$
m+1	1	m+1	m-1	$\Phi_{m+1}(1)=(1/4)[\Phi_m(m-2)+2\Phi_m(1)+\Phi_m(m)]$
.	.	.	.	. . . .
.	.	.	.	. . . .
n-3	1	n-3	3	$\Phi_{n-3}(1)=(1/4)[\Phi_{n-4}(2)+2\Phi_{n-4}(1)+\Phi_{n-4}(4)]$
n-2	1	n-2	2	$\Phi_{n-2}(1)=(1/4)[\Phi_{n-3}(1)+2\Phi_{n-3}(1)+\Phi_{n-3}(3)]$
n-1	1	n-1	1	$\Phi_{n-1}(1)=(1/4)[\Phi_{n-2}(0)+2\Phi_{n-2}(1)+\Phi_{n-2}(2)]$
n	2	1	1	$\Phi_n(1)=(1/4)[\Phi_{n-1}(0)+2\Phi_{n-1}(1)+\Phi_{n-1}(2)]$
n+1	2	2	2	$\Phi_{n+1}(1)=(1/4)[\Phi_n(1)+2\Phi_n(1)+\Phi_n(3)]$
n+2	2	3	3	$\Phi_{n+2}(1)=(1/4)[\Phi_{n+1}(2)+2\Phi_{n+1}(1)+\Phi_{n+1}(4)]$
.	.	.	.	. . . .
.	.	.	.	. . . .

For the description of the symbols see Appendix Table 1.

Appendix Table 7

Recurrence equations for coefficient of identity of individuals born in cages two steps apart in successive generations for odd values of n

t	c	t'	i	Equation
1	1	1	1	$\Phi_1(2)=(1/4)[\Phi_0(1)+2\Phi_0(2)+\Phi_0(3)]$
2	1	2	2	$\Phi_2(2)=(1/4)[\Phi_1(0)+2\Phi_1(2)+\Phi_1(4)]$
3	1	3	3	$\Phi_3(2)=(1/4)[\Phi_2(1)+2\Phi_2(2)+\Phi_2(5)]$
4	1	4	4	$\Phi_3(2)=(1/4)[\Phi_2(2)+2\Phi_2(2)+\Phi_2(6)]$
.	.	.	.	. . . .
.	.	.	.	. . . .
m-1	1	m-1	m-1	$\Phi_{m-1}(2)=(1/4)[\Phi_{m-2}(m-3)+2\Phi_{m-2}(2)+\Phi_{m-2}(m+1)]$
m	1	m	m	$\Phi_m(2)=(1/4)[\Phi_{m-1}(m-2)+2\Phi_{m-1}(2)+\Phi_{m-1}(m+2)]$
m+1	1	m+1	m	$\Phi_{m+1}(2)=(1/4)[\Phi_m(m-2)+2\Phi_m(2)+\Phi_m(m+2)]$
m+2	1	m+2	m-1	$\Phi_{m+2}(2)=(1/4)[\Phi_{m+1}(m-3)+2\Phi_{m+1}(2)+\Phi_{m+1}(m+1)]$
.	.	.	.	. . . .
.	.	.	.	. . . .
n-4	1	n-4	4	$\Phi_{n-2}(2)=(1/4)[\Phi_{n-5}(2)+2\Phi_{n-5}(2)+\Phi_{n-4}(2)]$
n-3	1	n-3	3	$\Phi_{n-3}(2)=(1/4)[\Phi_{n-4}(1)+2\Phi_{n-4}(2)+\Phi_{n-4}(5)]$
n-2	1	n-2	2	$\Phi_{n-2}(2)=(1/4)[\Phi_{n-3}(0)+2\Phi_{n-3}(2)+\Phi_{n-3}(4)]$
n-1	1	n-1	1	$\Phi_{n-1}(2)=(1/4)[\Phi_{n-2}(1)+2\Phi_{n-2}(2)+\Phi_{n-2}(3)]$
n	2	1	1	$\Phi_n(2)=(1/4)[\Phi_{n-1}(1)+2\Phi_{n-1}(2)+\Phi_{n-1}(3)]$
n+1	2	2	2	$\Phi_{n+1}(2)=(1/4)[\Phi_n(0)+2\Phi_n(2)+\Phi_n(4)]$
n+2	2	3	3	$\Phi_{n+2}(2)=(1/4)[\Phi_{n+1}(2)+2\Phi_{n+1}(2)+\Phi_{n+1}(5)]$
.	.	.	.	. . . .
.	.	.	.	. . . .

For the description of the symbols see Appendix Table 1.

Appendix Table 8

Recurrence equations for coefficient of identity of individuals born in cages two steps apart in successive generations for even values of n

t	c	t'	i	Equation
1	1	1	1	$\Phi_1(2)=(1/4)[\Phi_0(1)+2\Phi_0(2)+\Phi_0(3)]$
2	1	2	2	$\Phi_2(2)=(1/4)[\Phi_1(0)+2\Phi_1(2)+\Phi_1(4)]$
3	1	3	3	$\Phi_3(2)=(1/4)[\Phi_2(1)+2\Phi_2(2)+\Phi_2(5)]$
4	1	4	4	$\Phi_3(2)=(1/4)[\Phi_2(2)+2\Phi_2(2)+\Phi_2(6)]$
.	.	.	.	. . . .
.	.	.	.	. . . .
m-1	1	m-1	m-1	$\Phi_{m-1}(2)=(1/4)[\Phi_{m-2}(m-3)+2\Phi_{m-2}(2)+\Phi_{m-2}(m+1)]$
m	1	m	m	$\Phi_m(2)=(1/4)[\Phi_{m-1}(m-2)+2\Phi_{m-1}(2)+\Phi_{m-1}(m+2)]$
m+1	1	m+1	m-1	$\Phi_{m+1}(2)=(1/4)[\Phi_m(m-3)+2\Phi_m(2)+\Phi_m(m+1)]$
.	.	.	.	. . . .
.	.	.	.	. . . .
n-4	1	n-4	4	$\Phi_{n-4}(2)=(1/4)[\Phi_{n-5}(2)+2\Phi_{n-5}(2)+\Phi_{n-2}(2)]$
n-3	1	n-3	3	$\Phi_{n-3}(2)=(1/4)[\Phi_{n-4}(1)+2\Phi_{n-4}(2)+\Phi_{n-4}(5)]$
n-2	1	n-2	2	$\Phi_{n-2}(2)=(1/4)[\Phi_{n-3}(0)+2\Phi_{n-3}(2)+\Phi_{n-3}(4)]$
n-1	1	n-1	1	$\Phi_{n-1}(2)=(1/4)[\Phi_{n-2}(1)+2\Phi_{n-2}(2)+\Phi_{n-2}(3)]$
n	2	1	1	$\Phi_n(2)=(1/4)[\Phi_{n-1}(1)+2\Phi_{n-1}(2)+\Phi_{n-1}(3)]$
n+1	2	2	2	$\Phi_{n+1}(2)=(1/4)[\Phi_n(0)+2\Phi_n(2)+\Phi_n(4)]$
n+2	2	3	3	$\Phi_{n+2}(2)=(1/4)[\Phi_{n+1}(2)+2\Phi_{n+1}(2)+\Phi_{n+1}(5)]$
.	.	.	.	. . . .
.	.	.	.	. . . .

For the description of the symbols see Appendix Table 1.

APPENDIX III.2. Examples of the generation matrices

Generation matrices for population of size 30
(n=15, m=7)†

G_1

$$\begin{vmatrix} H_t \\ \Psi_t(0) \\ \Psi_t(1) \\ \Psi_t(2) \\ \Psi_t(3) \\ \Psi_t(4) \\ \Psi_t(5) \\ \Psi_t(6) \\ \Psi_t(7) \end{vmatrix} = \begin{vmatrix} 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ .25 & 0 & .5 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & .25 & .5 & .25 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & .25 & .5 & .25 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & .25 & .5 & .25 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & .25 & .5 & .25 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & .25 & .5 & .25 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & .25 & .5 & .25 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & .25 & .75 \end{vmatrix} \begin{vmatrix} H_{t-1} \\ \Psi_{t-1}(0) \\ \Psi_{t-1}(1) \\ \Psi_{t-1}(2) \\ \Psi_{t-1}(3) \\ \Psi_{t-1}(4) \\ \Psi_{t-1}(5) \\ \Psi_{t-1}(6) \\ \Psi_{t-1}(7) \end{vmatrix}$$

G_2

$$\begin{vmatrix} H_t \\ \Psi_t(0) \\ \Psi_t(1) \\ \Psi_t(2) \\ \Psi_t(3) \\ \Psi_t(4) \\ \Psi_t(5) \\ \Psi_t(6) \\ \Psi_t(7) \end{vmatrix} = \begin{vmatrix} 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ .25 & 0 & 0 & .5 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & .75 & 0 & .25 & 0 & 0 & 0 & 0 \\ 0 & .25 & 0 & .5 & 0 & .25 & 0 & 0 & 0 \\ 0 & 0 & .25 & 0 & .5 & 0 & .25 & 0 & 0 \\ 0 & 0 & 0 & .25 & 0 & .5 & 0 & .25 & 0 \\ 0 & 0 & 0 & 0 & .25 & 0 & .5 & 0 & .25 \\ 0 & 0 & 0 & 0 & 0 & .25 & 0 & .5 & .25 \\ 0 & 0 & 0 & 0 & 0 & 0 & .25 & .25 & .5 \end{vmatrix} \begin{vmatrix} H_{t-1} \\ \Psi_{t-1}(0) \\ \Psi_{t-1}(1) \\ \Psi_{t-1}(2) \\ \Psi_{t-1}(3) \\ \Psi_{t-1}(4) \\ \Psi_{t-1}(5) \\ \Psi_{t-1}(6) \\ \Psi_{t-1}(7) \end{vmatrix}$$

G_3

$$\begin{vmatrix} H_t \\ \Psi_t(0) \\ \Psi_t(1) \\ \Psi_t(2) \\ \Psi_t(3) \\ \Psi_t(4) \\ \Psi_t(5) \\ \Psi_t(6) \\ \Psi_t(7) \end{vmatrix} = \begin{vmatrix} 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ .25 & 0 & 0 & 0 & .5 & 0 & 0 & 0 & 0 \\ 0 & 0 & .5 & .25 & 0 & .25 & 0 & 0 & 0 \\ 0 & 0 & .25 & .5 & 0 & 0 & .25 & 0 & 0 \\ 0 & .25 & 0 & 0 & .5 & 0 & 0 & .25 & 0 \\ 0 & 0 & .25 & 0 & 0 & .5 & 0 & 0 & .25 \\ 0 & 0 & 0 & .25 & 0 & 0 & .5 & 0 & .25 \\ 0 & 0 & 0 & 0 & .25 & 0 & 0 & .75 & 0 \\ 0 & 0 & 0 & 0 & 0 & .25 & .25 & 0 & .5 \end{vmatrix} \begin{vmatrix} H_{t-1} \\ \Psi_{t-1}(0) \\ \Psi_{t-1}(1) \\ \Psi_{t-1}(2) \\ \Psi_{t-1}(3) \\ \Psi_{t-1}(4) \\ \Psi_{t-1}(5) \\ \Psi_{t-1}(6) \\ \Psi_{t-1}(7) \end{vmatrix}$$

---

† n and m are the number of pair matings and different types of matrices respectively.

The integer numbers within parenthesis indicate the number of steps between cages.

Generation matrices for population of size 30 (Continued)

$$G_4$$

$$\begin{vmatrix} H_t \\ \Psi_t(0) \\ \Psi_t(1) \\ \Psi_t(2) \\ \Psi_t(3) \\ \Psi_t(4) \\ \Psi_t(5) \\ \Psi_t(6) \\ \Psi_t(7) \end{vmatrix} = \begin{vmatrix} 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ .25 & 0 & 0 & 0 & 0 & .5 & 0 & 0 & 0 \\ 0 & 0 & .5 & 0 & .25 & 0 & .25 & 0 & 0 \\ 0 & 0 & 0 & .75 & 0 & 0 & 0 & .25 & 0 \\ 0 & 0 & .25 & 0 & .5 & 0 & 0 & 0 & .25 \\ 0 & .25 & 0 & 0 & 0 & .5 & 0 & 0 & .25 \\ 0 & 0 & .25 & 0 & 0 & 0 & .5 & .25 & 0 \\ 0 & 0 & 0 & .25 & 0 & 0 & .25 & .5 & 0 \\ 0 & 0 & 0 & 0 & .25 & .25 & 0 & 0 & .5 \end{vmatrix} \begin{vmatrix} H_{t-1} \\ \Psi_{t-1}(0) \\ \Psi_{t-1}(1) \\ \Psi_{t-1}(2) \\ \Psi_{t-1}(3) \\ \Psi_{t-1}(4) \\ \Psi_{t-1}(5) \\ \Psi_{t-1}(6) \\ \Psi_{t-1}(7) \end{vmatrix}$$

$$G_5$$

$$\begin{vmatrix} H_t \\ \Psi_t(0) \\ \Psi_t(1) \\ \Psi_t(2) \\ \Psi_t(3) \\ \Psi_t(4) \\ \Psi_t(5) \\ \Psi_t(6) \\ \Psi_t(7) \end{vmatrix} = \begin{vmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ .25 & 0 & 0 & 0 & 0 & 0 & .5 & 0 & 0 \\ 0 & 0 & .5 & 0 & 0 & .25 & 0 & .25 & 0 \\ 0 & 0 & 0 & .5 & .25 & 0 & 0 & 0 & .25 \\ 0 & 0 & 0 & .25 & .5 & 0 & 0 & 0 & .25 \\ 0 & 0 & .25 & 0 & 0 & .5 & 0 & .25 & 0 \\ 0 & .25 & 0 & 0 & 0 & 0 & .75 & 0 & 0 \\ 0 & 0 & .25 & 0 & 0 & .25 & 0 & .5 & 0 \\ 0 & 0 & 0 & .25 & .25 & 0 & 0 & 0 & .5 \end{vmatrix} \begin{vmatrix} H_{t-1} \\ \Psi_{t-1}(0) \\ \Psi_{t-1}(1) \\ \Psi_{t-1}(2) \\ \Psi_{t-1}(3) \\ \Psi_{t-1}(4) \\ \Psi_{t-1}(5) \\ \Psi_{t-1}(6) \\ \Psi_{t-1}(7) \end{vmatrix}$$

$$G_6$$

$$\begin{vmatrix} H_t \\ \Psi_t(0) \\ \Psi_t(1) \\ \Psi_t(2) \\ \Psi_t(3) \\ \Psi_t(4) \\ \Psi_t(5) \\ \Psi_t(6) \\ \Psi_t(7) \end{vmatrix} = \begin{vmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ .25 & 0 & 0 & 0 & 0 & 0 & 0 & .5 & 0 \\ 0 & 0 & .5 & 0 & 0 & 0 & .25 & 0 & .25 \\ 0 & 0 & 0 & .5 & 0 & .25 & 0 & 0 & .25 \\ 0 & 0 & 0 & 0 & .75 & 0 & 0 & .25 & 0 \\ 0 & 0 & 0 & .25 & 0 & .5 & .25 & 0 & 0 \\ 0 & 0 & .25 & 0 & 0 & .25 & .5 & 0 & 0 \\ 0 & .25 & 0 & 0 & .25 & 0 & 0 & .5 & 0 \\ 0 & 0 & .25 & .25 & 0 & 0 & 0 & 0 & .5 \end{vmatrix} \begin{vmatrix} H_{t-1} \\ \Psi_{t-1}(0) \\ \Psi_{t-1}(1) \\ \Psi_{t-1}(2) \\ \Psi_{t-1}(3) \\ \Psi_{t-1}(4) \\ \Psi_{t-1}(5) \\ \Psi_{t-1}(6) \\ \Psi_{t-1}(7) \end{vmatrix}$$

$$G_7$$

$$\begin{vmatrix} H_t \\ \Psi_t(0) \\ \Psi_t(1) \\ \Psi_t(2) \\ \Psi_t(3) \\ \Psi_t(4) \\ \Psi_t(5) \\ \Psi_t(6) \\ \Psi_t(7) \end{vmatrix} = \begin{vmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \\ .25 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & .5 \\ 0 & 0 & .5 & 0 & 0 & 0 & 0 & .25 & .25 \\ 0 & 0 & 0 & .5 & 0 & 0 & .25 & .25 & 0 \\ 0 & 0 & 0 & 0 & .5 & .25 & .25 & 0 & 0 \\ 0 & 0 & 0 & 0 & .25 & .75 & 0 & 0 & 0 \\ 0 & 0 & 0 & .25 & .25 & 0 & .5 & 0 & 0 \\ 0 & 0 & .25 & .25 & 0 & 0 & 0 & .5 & 0 \\ 0 & .25 & .25 & 0 & 0 & 0 & 0 & 0 & .5 \end{vmatrix} \begin{vmatrix} H_{t-1} \\ \Psi_{t-1}(0) \\ \Psi_{t-1}(1) \\ \Psi_{t-1}(2) \\ \Psi_{t-1}(3) \\ \Psi_{t-1}(4) \\ \Psi_{t-1}(5) \\ \Psi_{t-1}(6) \\ \Psi_{t-1}(7) \end{vmatrix}$$

Generation matrices for population of size 32 (n=16, m=8)

$$G_1$$

$$\begin{vmatrix} H_t \\ \Psi_t(0) \\ \Psi_t(1) \\ \Psi_t(2) \\ \Psi_t(3) \\ \Psi_t(4) \\ \Psi_t(5) \\ \Psi_t(6) \\ \Psi_t(7) \\ \Psi_t(8) \end{vmatrix} = \begin{vmatrix} 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ .25 & 0 & .5 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & .25 & .5 & .25 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & .25 & .5 & .25 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & .25 & .5 & .25 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & .25 & .5 & .25 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & .25 & .5 & .25 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & .25 & .5 & .25 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & .25 & .5 & .25 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & .5 & .5 \end{vmatrix} \begin{vmatrix} H_{t-1} \\ \Psi_{t-1}(0) \\ \Psi_{t-1}(1) \\ \Psi_{t-1}(2) \\ \Psi_{t-1}(3) \\ \Psi_{t-1}(4) \\ \Psi_{t-1}(5) \\ \Psi_{t-1}(6) \\ \Psi_{t-1}(7) \\ \Psi_{t-1}(8) \end{vmatrix}$$

$$G_2$$

$$\begin{vmatrix} H_t \\ \Psi_t(0) \\ \Psi_t(1) \\ \Psi_t(2) \\ \Psi_t(3) \\ \Psi_t(4) \\ \Psi_t(5) \\ \Psi_t(6) \\ \Psi_t(7) \\ \Psi_t(8) \end{vmatrix} = \begin{vmatrix} 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ .25 & 0 & 0 & .5 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & .75 & 0 & .25 & 0 & 0 & 0 & 0 & 0 \\ 0 & .25 & 0 & .5 & 0 & .25 & 0 & 0 & 0 & 0 \\ 0 & 0 & .25 & 0 & .5 & 0 & .25 & 0 & 0 & 0 \\ 0 & 0 & 0 & .25 & 0 & .5 & 0 & .25 & 0 & 0 \\ 0 & 0 & 0 & 0 & .25 & 0 & .5 & 0 & .25 & 0 \\ 0 & 0 & 0 & 0 & 0 & .25 & 0 & .5 & 0 & .25 \\ 0 & 0 & 0 & 0 & 0 & 0 & .25 & 0 & .75 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & .5 & 0 & .5 \end{vmatrix} \begin{vmatrix} H_{t-1} \\ \Psi_{t-1}(0) \\ \Psi_{t-1}(1) \\ \Psi_{t-1}(2) \\ \Psi_{t-1}(3) \\ \Psi_{t-1}(4) \\ \Psi_{t-1}(5) \\ \Psi_{t-1}(6) \\ \Psi_{t-1}(7) \\ \Psi_{t-1}(8) \end{vmatrix}$$

$$G_3$$

$$\begin{vmatrix} H_t \\ \Psi_t(0) \\ \Psi_t(1) \\ \Psi_t(2) \\ \Psi_t(3) \\ \Psi_t(4) \\ \Psi_t(5) \\ \Psi_t(6) \\ \Psi_t(7) \\ \Psi_t(8) \end{vmatrix} = \begin{vmatrix} 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ .25 & 0 & 0 & 0 & .5 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & .5 & .25 & 0 & .25 & 0 & 0 & 0 & 0 \\ 0 & 0 & .25 & .5 & 0 & 0 & .25 & 0 & 0 & 0 \\ 0 & .25 & 0 & 0 & .5 & 0 & 0 & .25 & 0 & 0 \\ 0 & 0 & .25 & 0 & 0 & .5 & 0 & 0 & .25 & 0 \\ 0 & 0 & 0 & .25 & 0 & 0 & .5 & 0 & 0 & .25 \\ 0 & 0 & 0 & 0 & .25 & 0 & 0 & .5 & .25 & 0 \\ 0 & 0 & 0 & 0 & 0 & .25 & 0 & .25 & .5 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & .5 & 0 & 0 & .5 \end{vmatrix} \begin{vmatrix} H_{t-1} \\ \Psi_{t-1}(0) \\ \Psi_{t-1}(1) \\ \Psi_{t-1}(2) \\ \Psi_{t-1}(3) \\ \Psi_{t-1}(4) \\ \Psi_{t-1}(5) \\ \Psi_{t-1}(6) \\ \Psi_{t-1}(7) \\ \Psi_{t-1}(8) \end{vmatrix}$$

$$G_4$$

$$\begin{vmatrix} H_t \\ \Psi_t(0) \\ \Psi_t(1) \\ \Psi_t(2) \\ \Psi_t(3) \\ \Psi_t(4) \\ \Psi_t(5) \\ \Psi_t(6) \\ \Psi_t(7) \\ \Psi_t(8) \end{vmatrix} = \begin{vmatrix} 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ .25 & 0 & 0 & 0 & 0 & .5 & 0 & 0 & 0 & 0 \\ 0 & 0 & .5 & 0 & .25 & 0 & .25 & 0 & 0 & 0 \\ 0 & 0 & 0 & .75 & 0 & 0 & 0 & .25 & 0 & 0 \\ 0 & 0 & .25 & 0 & .5 & 0 & 0 & 0 & .25 & 0 \\ 0 & .25 & 0 & 0 & 0 & .5 & 0 & 0 & 0 & .25 \\ 0 & 0 & .25 & 0 & 0 & 0 & .5 & 0 & .25 & 0 \\ 0 & 0 & 0 & .25 & 0 & 0 & 0 & .75 & 0 & 0 \\ 0 & 0 & 0 & 0 & .25 & 0 & .25 & 0 & .5 & 0 \\ 0 & 0 & 0 & 0 & 0 & .5 & 0 & 0 & 0 & .5 \end{vmatrix} \begin{vmatrix} H_{t-1} \\ \Psi_{t-1}(0) \\ \Psi_{t-1}(1) \\ \Psi_{t-1}(2) \\ \Psi_{t-1}(3) \\ \Psi_{t-1}(4) \\ \Psi_{t-1}(5) \\ \Psi_{t-1}(6) \\ \Psi_{t-1}(7) \\ \Psi_{t-1}(8) \end{vmatrix}$$

Generation matrices for population of size 32 (Continued)

$$G_5$$

$$\begin{vmatrix} H_t \\ \Psi_t(0) \\ \Psi_t(1) \\ \Psi_t(2) \\ \Psi_t(3) \\ \Psi_t(4) \\ \Psi_t(5) \\ \Psi_t(6) \\ \Psi_t(7) \\ \Psi_t(8) \end{vmatrix} = \begin{vmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ .25 & 0 & 0 & 0 & 0 & 0 & .5 & 0 & 0 & 0 \\ 0 & 0 & .5 & 0 & 0 & .25 & 0 & .25 & 0 & 0 \\ 0 & 0 & 0 & .5 & .25 & 0 & 0 & 0 & .25 & 0 \\ 0 & 0 & 0 & .25 & .5 & 0 & 0 & 0 & 0 & .25 \\ 0 & 0 & .25 & 0 & 0 & .5 & 0 & 0 & .25 & 0 \\ 0 & .25 & 0 & 0 & 0 & 0 & .5 & .25 & 0 & 0 \\ 0 & 0 & .25 & 0 & 0 & 0 & .25 & .5 & 0 & 0 \\ 0 & 0 & 0 & .25 & 0 & .25 & 0 & 0 & .5 & 0 \\ 0 & 0 & 0 & 0 & .5 & 0 & 0 & 0 & 0 & .5 \end{vmatrix} \begin{vmatrix} H_{t-1} \\ \Psi_{t-1}(0) \\ \Psi_{t-1}(1) \\ \Psi_{t-1}(2) \\ \Psi_{t-1}(3) \\ \Psi_{t-1}(4) \\ \Psi_{t-1}(5) \\ \Psi_{t-1}(6) \\ \Psi_{t-1}(7) \\ \Psi_{t-1}(8) \end{vmatrix}$$

$$G_6$$

$$\begin{vmatrix} H_t \\ \Psi_t(0) \\ \Psi_t(1) \\ \Psi_t(2) \\ \Psi_t(3) \\ \Psi_t(4) \\ \Psi_t(5) \\ \Psi_t(6) \\ \Psi_t(7) \\ \Psi_t(8) \end{vmatrix} = \begin{vmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ .25 & 0 & 0 & 0 & 0 & 0 & 0 & .5 & 0 & 0 \\ 0 & 0 & .5 & 0 & 0 & 0 & .25 & 0 & .25 & 0 \\ 0 & 0 & 0 & .5 & 0 & .25 & 0 & 0 & 0 & .25 \\ 0 & 0 & 0 & 0 & .75 & 0 & 0 & 0 & .25 & 0 \\ 0 & 0 & 0 & .25 & 0 & .5 & 0 & .25 & 0 & 0 \\ 0 & 0 & .25 & 0 & 0 & 0 & .75 & 0 & 0 & 0 \\ 0 & .25 & 0 & 0 & 0 & .25 & 0 & .5 & 0 & 0 \\ 0 & 0 & .25 & 0 & .25 & 0 & 0 & 0 & .5 & 0 \\ 0 & 0 & 0 & .5 & 0 & 0 & 0 & 0 & 0 & .5 \end{vmatrix} \begin{vmatrix} H_{t-1} \\ \Psi_{t-1}(0) \\ \Psi_{t-1}(1) \\ \Psi_{t-1}(2) \\ \Psi_{t-1}(3) \\ \Psi_{t-1}(4) \\ \Psi_{t-1}(5) \\ \Psi_{t-1}(6) \\ \Psi_{t-1}(7) \\ \Psi_{t-1}(8) \end{vmatrix}$$

$$G_7$$

$$\begin{vmatrix} H_t \\ \Psi_t(0) \\ \Psi_t(1) \\ \Psi_t(2) \\ \Psi_t(3) \\ \Psi_t(4) \\ \Psi_t(5) \\ \Psi_t(6) \\ \Psi_t(7) \\ \Psi_t(8) \end{vmatrix} = \begin{vmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ .25 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & .5 & 0 \\ 0 & 0 & .5 & 0 & 0 & 0 & 0 & .25 & 0 & .25 \\ 0 & 0 & 0 & .5 & 0 & 0 & .25 & 0 & .25 & 0 \\ 0 & 0 & 0 & 0 & .5 & .25 & 0 & .25 & 0 & 0 \\ 0 & 0 & 0 & 0 & .25 & .5 & .25 & 0 & 0 & 0 \\ 0 & 0 & 0 & .25 & 0 & .25 & .5 & 0 & 0 & 0 \\ 0 & 0 & .25 & 0 & .25 & 0 & 0 & .5 & 0 & 0 \\ 0 & .25 & 0 & .25 & 0 & 0 & 0 & 0 & .5 & 0 \\ 0 & 0 & .5 & 0 & 0 & 0 & 0 & 0 & 0 & .5 \end{vmatrix} \begin{vmatrix} H_{t-1} \\ \Psi_{t-1}(0) \\ \Psi_{t-1}(1) \\ \Psi_{t-1}(2) \\ \Psi_{t-1}(3) \\ \Psi_{t-1}(4) \\ \Psi_{t-1}(5) \\ \Psi_{t-1}(6) \\ \Psi_{t-1}(7) \\ \Psi_{t-1}(8) \end{vmatrix}$$

$$G_8$$

$$\begin{vmatrix} H_t \\ \Psi_t(0) \\ \Psi_t(1) \\ \Psi_t(2) \\ \Psi_t(3) \\ \Psi_t(4) \\ \Psi_t(5) \\ \Psi_t(6) \\ \Psi_t(7) \\ \Psi_t(8) \end{vmatrix} = \begin{vmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \\ .25 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & .5 \\ 0 & 0 & .5 & 0 & 0 & 0 & 0 & 0 & .5 & 0 \\ 0 & 0 & 0 & .5 & 0 & 0 & 0 & .5 & 0 & 0 \\ 0 & 0 & 0 & 0 & .5 & 0 & .5 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & .5 & 0 & .5 & 0 & 0 & 0 \\ 0 & 0 & 0 & .5 & 0 & 0 & 0 & .5 & 0 & 0 \\ 0 & 0 & .5 & 0 & 0 & 0 & 0 & 0 & .5 & 0 \\ 0 & .5 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & .5 \end{vmatrix} \begin{vmatrix} H_{t-1} \\ \Psi_{t-1}(0) \\ \Psi_{t-1}(1) \\ \Psi_{t-1}(2) \\ \Psi_{t-1}(3) \\ \Psi_{t-1}(4) \\ \Psi_{t-1}(5) \\ \Psi_{t-1}(6) \\ \Psi_{t-1}(7) \\ \Psi_{t-1}(8) \end{vmatrix}$$

APPENDIX III-3. The relationships between generation matrices

The presence of a pattern between different generation matrices for each population size is evident (Appendix III-2). For example; let an element in the i-th row and j-th column of a generation matrix be g_{ij}. The g_{1j}=1 for j=3,4, . . m in the first, second, and the m-th matrix within each cycle. g_{21}=0.25 in all the matrices, and g_{2j}=0.5 for j=3,4, . . m in the first, second, and the m-th matrix (right below the 1 in the first row). The first matrix within each cycle is tri-diagonal and the elements in both sides of the main diagonal in the second, third, and the m-th matix move one, two and m columns away from the main diagonal. The object of this Appendix is to study the underlying relationships between the generation matrices for each population size, and to formulate the relationships such that all the matrices can be generated from as few matrices as possible. The discussion of this section would become more clear with the following definitions.

Circulant matrix: A circulant matrix is one in which a basic row of numbers is repeated again and again, but with a shift in position (Davis, 1979).

Permutation matrix: A permutation matrix is one which has precisely one 1 in each of its rows and columns, and zero elsewhere. Permutation matrices have the following properties:

$$PP'=P'P = P^nP^{n\prime}= P^{n\prime}P^n=I$$

$$P'=P^{-1}$$

(P' is transpose of P, P^{-1} is the inverse of P and I is an identity matrix). Thus P is an orthogonal and also a unitary matrix forming a subgroup of unitary group. The largest eigenvalue of P is one (Davis, 1979).

Congruent modulo: Let a, b and n be integers with $n > 0$. Then a and b are said to be *Congruent modulo* n , denoted by $a \equiv b(\text{mod } n)$, provided that $a-b$ is divisible by n; i.e. b is the residue of a/n (Adams and Goldstein, 1976). For example, $8 \equiv 3(\text{mod } 5)$. The number n is called the *modulus of the congruence*.

Primitive roots: Let m and n be relatively prime integers, with $n \geq 1$, and consider all the positive powers of m (m, m^2, m^3, m^4, . . .). It can be proved that:

$$_{m}\delta^{(n)} \equiv 1(\text{mod } n)$$

We are interested in the smallest positive integer k such that $m^k \equiv 1$ (mod n), which is called the exponent of m modulo n, and denoted by $k=exp_n(m)$. If $exp_n(m)=\delta(n)$, then m is called *primitive root mod n* (Apostol, 1976). The following example may be helpful in the clarification of this definition. Suppose $n=7$, then we have the following table for m^k of (mod 7):

m	K=0	1	2	3	4	5	6
0	0	0	0	0	0	0	0
1	1	1	1	1	1	1	1
2	1	2	4	1	2	4	1
3	1	3	2	6	4	5	1
4	1	4	2	1	4	2	1
5	1	5	4	6	2	3	1
6	1	6	1	6	1	6	1

This table shows that there are two integer values of m, 3 and 5, which have all the integers one through $n-1$ (1 to 6 in this case) as powers of them. It can be proved that for every prime number m there are such integers, which are called primitive roots. The smallest value (3 in the example) is the least positive primitive root of n (7 in this example). The reason that the maximum value of k was n-1=6 is that if $m^k \equiv 1$ (mod 7), then $m^{k+1} = m^k\ m \equiv m$(mod 7), and so forth. Thus, the powers repeat themselves when the exponent changes modulo 6. The least positive and least negative primitive roots of numbers can be found in Abramowitz and Stegun (1970).

It should be noted that the eigenvalues of the matrices which can be transformed to each other are identical, but elements of eigenvectors, eventhough identical in magnitude and sign, are in different orders in different matrices. In other words, generation matrices for each population can be transformed to one another if and only if their eigenvalues are the same. The number of unit eigenvalues (if they exist) and the largest non-unit eigenvalue of the generation matrices for populations of size 8 to 52 are shown in

Appendix Tables 9 and 10. From these Tables it is possible to easily identify the matrices which can be transformed to one another.

Ignoring the first two rows of the generation matrices, many of them are circulants. This suggests that there are permutation matrices which can be used to transform one to the other. Inspection of the generation matrices showed that the type of transformation of one matrix to another, and the corresponding permutation matrices share some similarities depending on whether n or n/2 are odd or even (n is the number of pairs of animals in the mating system), each case will be considered separately.

A-Cases where n is odd:

The permutation matrix (P) when n is odd has the following general form:

$$\begin{vmatrix}
1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & . & . \\
0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & . & . \\
0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & . & . \\
0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & . & . \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & . & . \\
. & . & . & . & . & . & . & . & . & . & . \\
. & . & . & . & . & . & . & . & . & . & . \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & . & . \\
0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & . & . \\
0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & . & . \\
0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & . & .
\end{vmatrix}$$

The column number in which 1's appear in the first, second, third, . . . s-3, s-2, s-1, and s-th rows (s is the size of the matrix and is equal to (n+3)/2 in this case) are 1, 2,

Appendix Table 9

The number of unit eigenvalues (λ_1) and the largest non-unit eigenvalue (λ_m) of the generation matrices (G_i) for populations of size 8 to 32

n	m	i	λ_1	λ_m	i	λ_1	λ_m
4	2	1	0	.965252	2	1	.919643
5	2	1,2	0	.973696			
6	3	1	0	.979163	2	1	.950647
		3	1	.919643			
7	3	1,2,3	0	.982968			
8	4	1,3	0	.986752	2	1	.965252
		4	1	.919643			
9	4	1,2,4	0	.987868	3	1	.950647
10	5	1,3	0	.989521	2,4	1	.973696
		5	2	.919643			
11	5	1 to 5	0	.990843			
12	6	1,5	0	.991920	2	1	.979163
		3	1	.965252	4	2	.950647
		6	3	.919643			
13	6	1 to 6	0	.992811			
14	7	1,3,5	0	.993557	2,4,6	1	.982968
		7	3	.919643			
15	7	1,2,4,7	0	.994190	3,6	1	.973696
		5	2	.950647			
16	8	1,3,5,7	0	.994732	2,6	1	.985752
		4	2	.965252	8	4	.919643

n and m are number of pairs of breeding individuals and different types of matrices respectively.

Appendix Table 10

The number of unit eigenvalues (λ_1) and the largest non-unit eignenvalue (λ_m) of the generation matrices (G_i) for populations of size 34 to 52

n	m	i	λ_1	λ_m	i	λ_1	λ_m
17	8	1 to 8	0	.995199			
18	9	1,5,7	0	.995606	2,4,6	1	.987868
		3	1	.979163	6	3	.950647
		9	4	.919643			
19	9	1 to 9	0	.995962			
20	10	1,3,7,9	0	.996276	2,6	1	.989521
		4,8	2	.973696	5	2	.965252
		10	5	.919643			
21	10	1,2,4,5,8,10	0	.996554	3,6,9	1	.982968
		7	3	.950647			
22	11	1,3,5,7,9	0	.996802	2,4,6,8,10	1	.990843
		11	5	.919643			
23	11	1 to 11	0	.997023			
24	12	1,5,7,11	0	.997222	2,10	1	.991920
		3,9	1	.985752	4	2	.979163
		6	3	.965252	8	4	.950647
		12	6	.919643			
25	12	1,2,3,4,6,7 8,9,11,12	0	.997402	5,10	2	.973696
26	13	1,3,5,7,9,11	0	.997564	13	6	.919643
		2,4,6,8,10,12	1	.992811			

n and m are number of pairs of breeding individuals and different types of matrices respectively.

4, 6, 8, . . . 9, 7, 5, 3. This permutation matrix can be partitioned as:

$$\left|\begin{array}{c|c} I & 0 \\ \hline 0' & Q \end{array}\right|$$

Where I is a 2 x 2 identity matrix, Q is a m x m matrix (m is different types of matrices within each cycle which is also equal to s-2), 0 is a 2 x m null matrix, and 0' is transpose of 0. Thus permutations of the form P'GP do not shift the first and second rows and columns of G, but other rows and columns (3, 4, ... m) are permutated by Q, which corresponds to Q(1)=2, Q(2)=4, Q(3)=6, . . . Q(m-2)=5, Q(m-1)=3 Q(m)=1. The correspondence between the sequence of permutation described above and the position of one's in the matrix Q is apparent. The above discussion in the matrix notation means that the matrix Q can be factored into a product of disjoint cycles, and this factorization is unique up to the arrangement of factors. For example; for N=22 (n=11, m=5), the permutation corresponds to Q(1)=2, Q(2)=4, Q(3)=5, Q(4)=3, Q(5)=1, which produces the full cycle 1 → 2 → 4 → 3 →5 →1. This permutation matrix is called primitive since its factorization consists of one cycle of full length m (Davis, 1979).

For N=30 (n=15, m=7), the permutation corresponds to Q(1)=2, Q(2)=4, Q(3)=6, Q(4)=7, Q(5)=5, Q(6)=3, Q(7)=1, showing that it is factorized into three disjoint cycles; (1 → 2 → 4 → 7 →1), (3 → 6 → 3) and (5 → 5). In general, when n is an odd prime, and one of its least positive or least negative primitive roots is even (n=5,7,11,13,19, etc.), then the corresponding permutation matrix is primitive. The transformation $P'G_xP=G_z$ gives exactly the same sequence of transformation of G_x to G_z within each cycle as shown above. For odd values of n, the general form of transformation of G_x to G_z, where $x=1,2,\ldots m$, is $z=\text{Minimum}[2x, n-2x]$, which gives both the number of groups and the sequence of transformation. For example, in the case of N=30 (n=15, m=7):

For $x=1$, $z=\text{Min}[2,13] \Rightarrow z=2 \Rightarrow G_1 \Rightarrow G_2$
For $x=2$, $z=\text{Min}[4,11] \Rightarrow z=4 \Rightarrow G_2 \Rightarrow G_4$
For $x=3$, $z=\text{Min}[6,9] \Rightarrow z=6 \Rightarrow G_3 \Rightarrow G_6$
For $x=4$, $z=\text{Min}[8,7] \Rightarrow z=7 \Rightarrow G_4 \Rightarrow G_7$
For $x=5$, $z=\text{Min}[10,5] \Rightarrow z=5 \Rightarrow G_5 \Rightarrow G_5$
For $x=6$, $z=\text{Min}[12,3] \Rightarrow z=3 \Rightarrow G_6 \Rightarrow G_3$
For $x=7$, $z=\text{Min}[14,1] \Rightarrow z=1 \Rightarrow G_7 \Rightarrow G_1$

The number of groups and the sequence of transformations under the operation $P'G_xP=G_z$ are shown in Appendix Table 11.

In addition to the above form of sequential transformation, any of the matrices in one group can be transformed to another matrix in the same group. There is an integer *d* which satisfies the relationship $P^d=I$ for all the permutation matrices. The values of *d* for different population sizes are shown in Appendix Table 12. The operation $P^yG_xP^{y'}= G_z$ or $P^{y'}G_xP^y=G_z$, where $y=1, 2, \ldots d-1$, will perform this transformation. Another property of the permutation matrices of this sort is $P^{\gamma}=P^{(d-\gamma)'}$. Appendix Table 12 shows that when n is an odd prime, and one of its least positive or least negative primitive roots is even (i.e. the corresponding permutation matrix is primitive) then *d=m*, and all the matrices for that population size can be transformed to each other. In other cases, *d<m* and the matrices form two or more groups. Examples of the transformation of the matrices into each other for a few odd values of n are presented in Appendix Table 13.

B-Cases where n is even and n/2 is odd:

The column number in which 1's appear in the first, second, . . . s-3, s-2, s-1 and s-th rows of the permutation matrix are 1, 2x1, s-2x1, 2x3, s-2x3, 2x5, s-2x5, 2x7 . . . s-2x6, 2x6, s-2x4, 2x4, s-2x2, 2x2, s; i.e., 1 in the odd rows are in columns 1, s-2, s-6, s-10, . . . s-12, s-8, s-4, s, and in even rows are in columns 2, 6, 10, 14, . . . 12, 8, 4. An example of the permutation matrices for the population size N=36 (n/2=9, s=11) is:

$$\begin{vmatrix}
1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\
0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1
\end{vmatrix}$$

Appendix Table 11

Groups of matrices and the sequence of transformation under the operation $P'G_xP=G_z$ for odd n's

n	m	Transformation
5	2	[1→2→1]
7	3	[1→2→3→1]
9	4	[1→2→4→1] [3→3]
11	5	[1→2→4→3→5→1]
13	6	[1→2→4→5→3→6→1]
15	7	[1→2→4→7→1] [3→6→3] [5→5]
17	8	[1→2→4→8→1] [3→6→5→7→3]
19	9	[1→2→4→8→3→6→7→5→9→ 1]
21	10	[1→2→4→8→5→10→1] [3→6→9→3] [7→7]
23	11	[1→2→4→8→7→9→5→10→3→6→11→1]
25	12	[1→2→4→8→9→7→11→3→6→12→1] [5→10→5]

n and m are number of pairs of breeding individuals and different types of matrices respectively.

Appendix Table 12

The values of *d* which satisfies $P^d=I$ for different n's

odd n's				even n's, odd n/2				even n's & n/2's			
n	m	s	d	n	m	s	d	n	m	s	d
5	2	4	2	6	3	5	1	4	2	4	1
7	3	5	3	10	5	7	2	8	4	6	2
9	4	6	3	14	7	9	3	12	6	8	2
11	5	7	5	18	9	11	3	16	8	10	4
13	6	8	6	22	11	13	5	20	10	12	4
15	7	9	4	26	13	15	6				
17	8	10	4	30	15	17	4				
19	9	11	9	34	17	19	4				
21	10	12	6	38	19	21	9				
23	11	13	11	42	21	23	6				
25	12	14	10	46	23	25	11				
27	13	15	9								
29	14	16	14								
31	15	17	5								
33	16	18	5								
35	17	19	12								
37	18	20	18								
39	19	21	12								
41	20	22	10								
43	21	23	7								
45	22	24	14								
47	23	25	23								

n, m and s are number of pairs of breeding individuals, different types of matrices within each cycle and size of matrices respectively.

P is permutation matrix and I is identity matrix

Appendix Table 13

Examples of transformation of generation matrices (G_i) using the permutation matrix P for odd values of n

n	m	Transformation
5	2	$G_2=PG_1P'=P'G_1P$ $G_1=PG_2P'=P'G_2P$
7	3	$G_2=P'G_1P=P^2G_1P^{2'}=PG_3P'$ $G_3=P^{2'}G_1P^2=PG_1P'=P'G_2P$ $G_1=PG_2P'=P'G_3P$
9	4	$G_2=P'G_1P=P^2G_1P^{2'}=PG_4P'$ $G_4=P'G_2P=P^{2'}G_1P^2=PG_1P'$ $G_3=PG_3P'=P^{2'}G_3P^2=P'G_3P=P^2G_3P^{2'}$
11	5	$G_2=P'G_1P=PG_4P'=P^2G_3P^{2'}=P^{2'}G_5P^2$ $G_3=P^{3'}G_1P^3=P^2G_1P^{2'}=P'G_4P=PG_5P'$ $G_4=P^{2'}G_1P^2=P'G_2P=PG_3P'=P^{2'}G_5P^{2'}$ $G_5=P^{4'}G_1P^4=PG_1P'=P'G_3P=P^{2'}G_2P^{2'}$
13	6	$G_2=P'G_1P=PG_4P'=P^{2'}G_6P^{2'}=P^{2'}G_5P^{2'}$ $G_2=P^{3'}G_3P^3$ $G_3=P^{4'}G_1P^4=P^2G_1P^{2'}=P'G_5P$ $G_3=PG_6P'=P^{2'}G_4P^2=P^{3'}G_2P^3$ $G_4=P^{2'}G_1P^2=P^{4'}G_1P^4=P'G_2P=PG_5P'$ $G_5=P^3G_1P^{3'}=P^{3'}G_1P^3=P'G_5P=PG_3P'$ $G_6=P^{5'}G_1P^5=PG_1P'=P'G_3P$

G_i's are generation matrices, P is permutation matrix, and P' is transpose of P.

The matrix $\mathbf{Q}$ corresponds to the permutation $Q(1)=m-2$, $Q(2)=4$, $Q(3)=m-6$, $Q(4)=8$, $Q(5)=m-10,\ldots$ $Q(m-3)=6$, $Q(m-2)=m-4$, $Q(m-1)=2$ and $Q(m)=m$. When $n/2$ is odd, d which satisfies $\mathbf{P}^d=\mathbf{I}$ is equal to $(n-2)/4$ if $n/2$ is an odd prime, and one of its least positive or least negative primitive roots is even. In such cases, the matrices form three distinct groups; $(1, 3, 5, \ldots m-2)$, $(2, 4, 6, \ldots m-1)$ and (m). In other cases $d<(n-2)/4$, and the matrices form more than three groups. Appendix Table 14 shows the number of groups and the sequence of transformation under the operation $\mathbf{P'GP}$.

C-Cases where n and n/2 are even:

The permutation matrices for the cases where both n and n/2 are even did not have a pattern such that a general form could be presented for different population sizes. The permutation matrices for populations of size 8 ($n=4$) to 40 ($n=20$) are shown below. The numbers in the body of the table are the column number in which 1 appears in the identified row of the permutation matrix.

	Row number											
n	1,	2,	3,	4,	5,	6,	7,	8,	9,	10,	11,	12
4	1,	2,	3,	4								
8	1,	2,	5,	4,	3,	6						
12	1,	2,	7,	4,	5,	6,	3,	8				
16	1,	2,	5,	8,	9,	6,	3,	4,	7,	10		
20	1,	2,	5,	8,	11,	10,	7,	4,	3,	6,	9,	12

Appendix Table 14

Groups of matrices and the sequence of transformation under the operation $P'G_xP=G_z$ for even n's

n	m	Transformation
		n/2 odd
6	3	[1⇒1] [2⇒2] [3⇒3]
10	5	[1⇒3⇒1] [2⇒4⇒2] [5⇒5]
14	7	[1⇒3⇒5⇒1] [2⇒6⇒4⇒2] [7⇒7]
18	9	[1⇒7⇒5⇒1] [2⇒4⇒8⇒2] [3⇒3] [6⇒6] [9⇒9]
22	11	[1⇒5⇒3⇒7⇒9⇒1] [2⇒10⇒6⇒8⇒4⇒2] [11⇒11]
26	13	[1⇒7⇒3⇒5⇒9⇒11⇒1] [2⇒12⇒6⇒10⇒8⇒4⇒2] [13⇒13]
		n/2 even
8	4	[1⇒3⇒1] [2⇒2] [4⇒4]
12	6	[1⇒5⇒1] [2⇒2] [3⇒3] [4⇒4] [6⇒6]
16	8	[1⇒5⇒7⇒3⇒1] [2⇒6⇒2] [4⇒4] [8⇒8]
20	10	[1⇒7⇒9⇒3⇒1] [2⇒6⇒2] [4⇒8⇒4] [5⇒5] [10⇒10]

n, m and s are number of pairs of breeding individuals, different types of matrices within each cycle and size of matrices respectively.

Appendix Table 15

The generation matrices (G_i) of different population sizes with the same largest non-unit eigenvalue (λ_m)

λ_m=.965252		.919643		.973696		.979163		.950647		.982968	
n	i	n	i	n	i	n	i	n	i	n	i
4	1	4	2	5	1,2	6	1	6	2	7	1,2,3
8	2	6	3	10	2,4	12	2	9	3	14	2,4,6
12	3	8	4	15	3,6	18	3	12	4	21	3,6,9
16	4	10	5	20	4,8	24	4	15	5		
20	5	12	6	25	5,1			18	6		
24	6	14	7					21	7		
		16	8					24	8		
		18	9								
		20	10								
		22	11								
		24	12								

n and i are number of pairs of breeding individuals and type of matrices within each population respectively.

The number of groups of matrices in this case is larger than those for the cases where n or n/2 were odd (Appendix Table 14), indicating that many of them cannot be transformed to each other. It should be noted that the permutation matrices were found by trial and error, and the process became extremely difficult and time consuming when the size of the matrices was large and n/2 was even.

Another interesting finding was the presence of a pattern between the eigenvalues of generation matrices of populations with different sizes. Examples of such patterns are illustarated in Appendix Table 15, which are largely self-explanatory. Inspection of the Appendix Tables 9 and 10 would reveal the existance of more such patterns. These patterns are useful in predicting the largest eigenvalues of many of the generation matrices of large dimensions without constructing them. For example, from Appendix Tables 9, 10 and 11, it is possible to write the largest eigenvalue of the following matrices in a population of size N=56 (n=28):

G_7: 1,1,1, .965252

G_{14}: 1,1,1,1,1,1,1 .919643

APPENDIX V.1 Frequency distributions of litter size in different populations

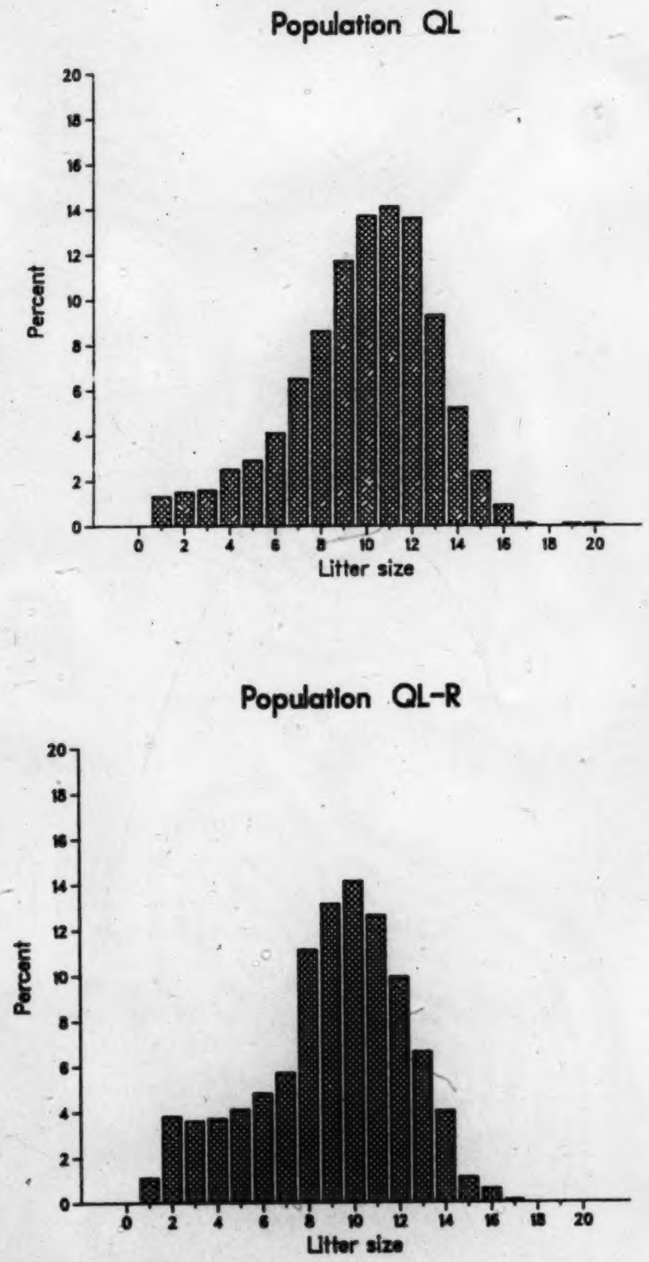


Figure 1. Frequency distributions of litter size in the QL and QL-R populations

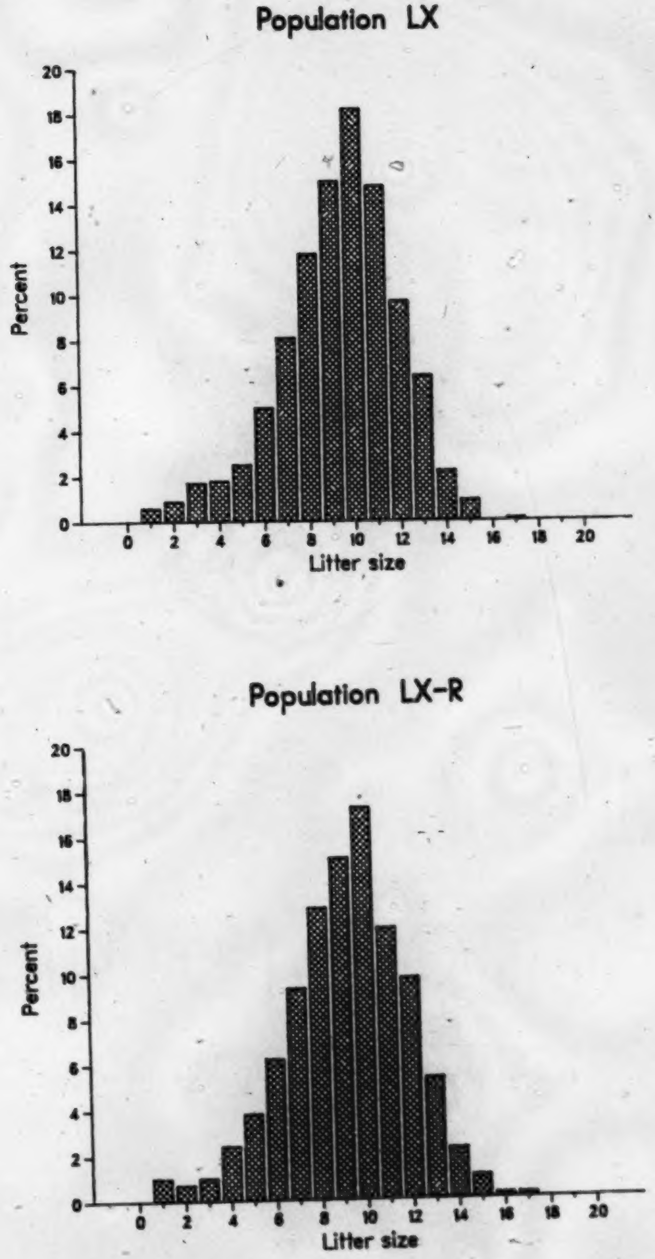


Figure 2. Frequency distributions of litter size in the LX and LX-R populations

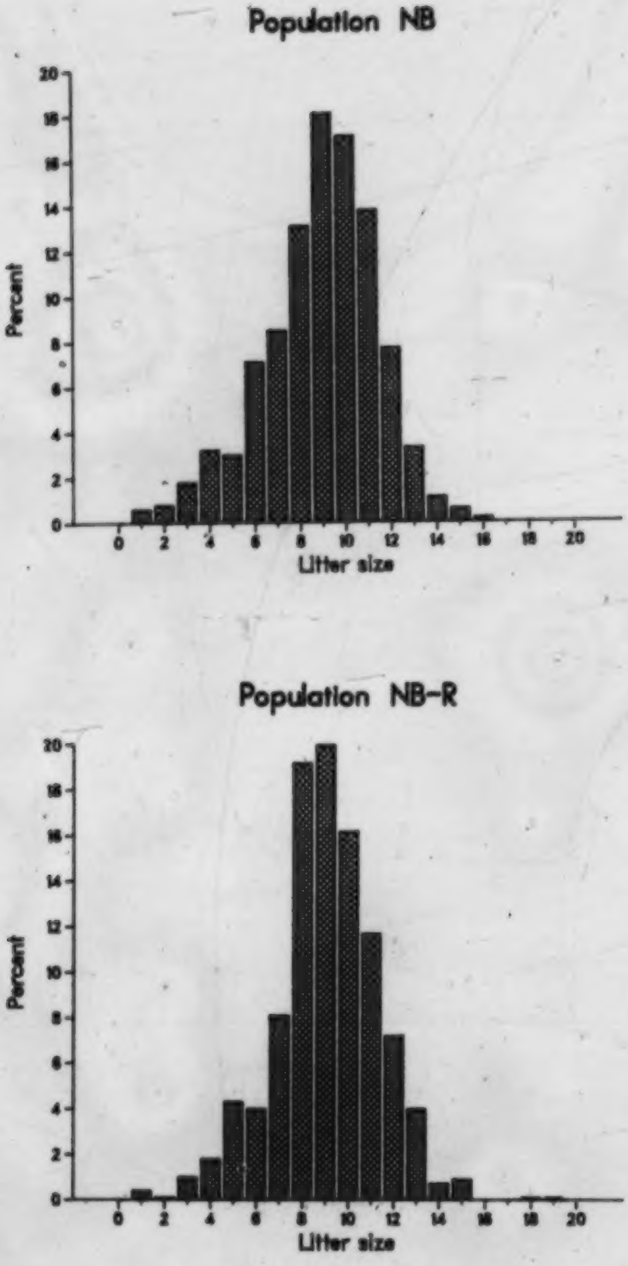
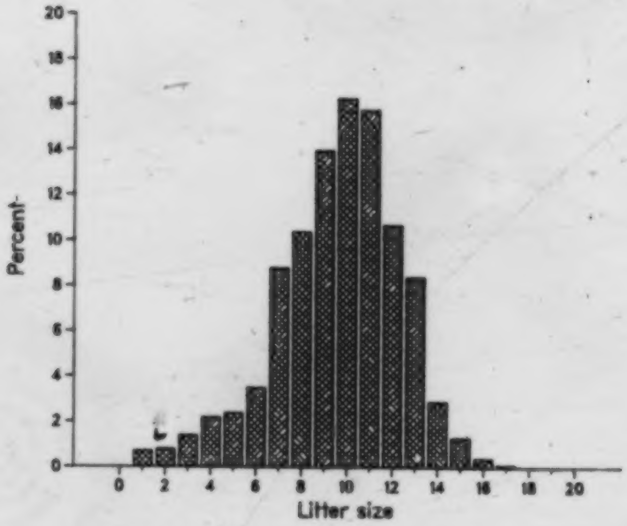


Figure 3. Frequency distributions of litter size in the NB and NB-R populations

Population OC



Population OC-R

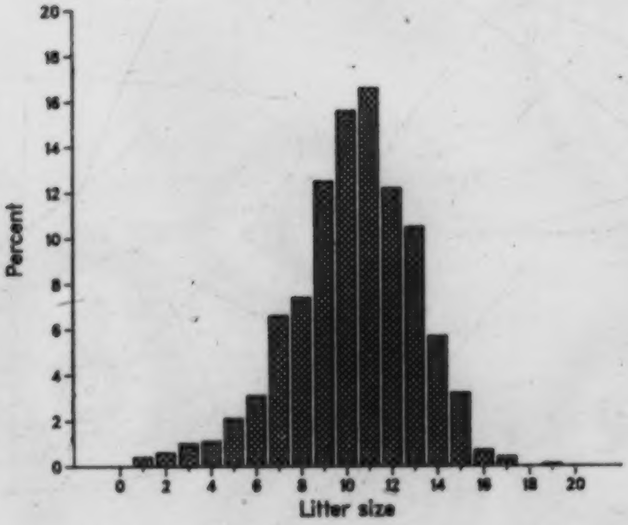


Figure 4. Frequency distributions of litter size in the OC and OC-R populations

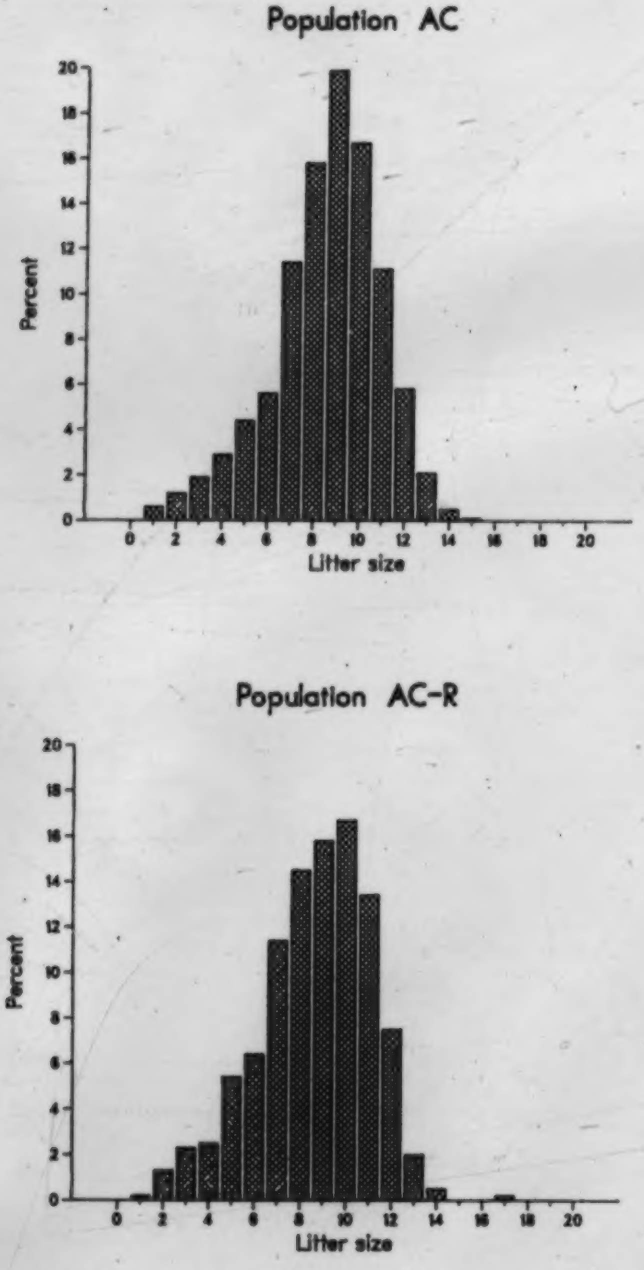
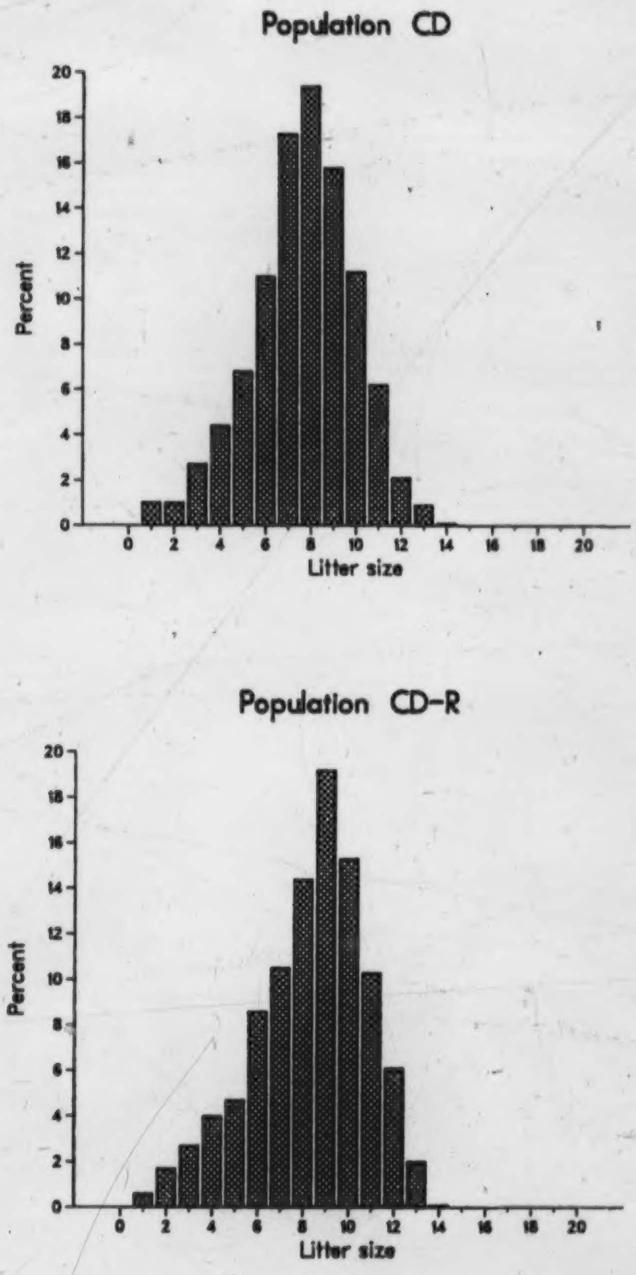


Figure 5. Frequency distributions of litter size in the AC and AC-R populations



Population CD

Population CD-R

Figure 6. Frequency distributions of litter size in the CD and CD-R populations

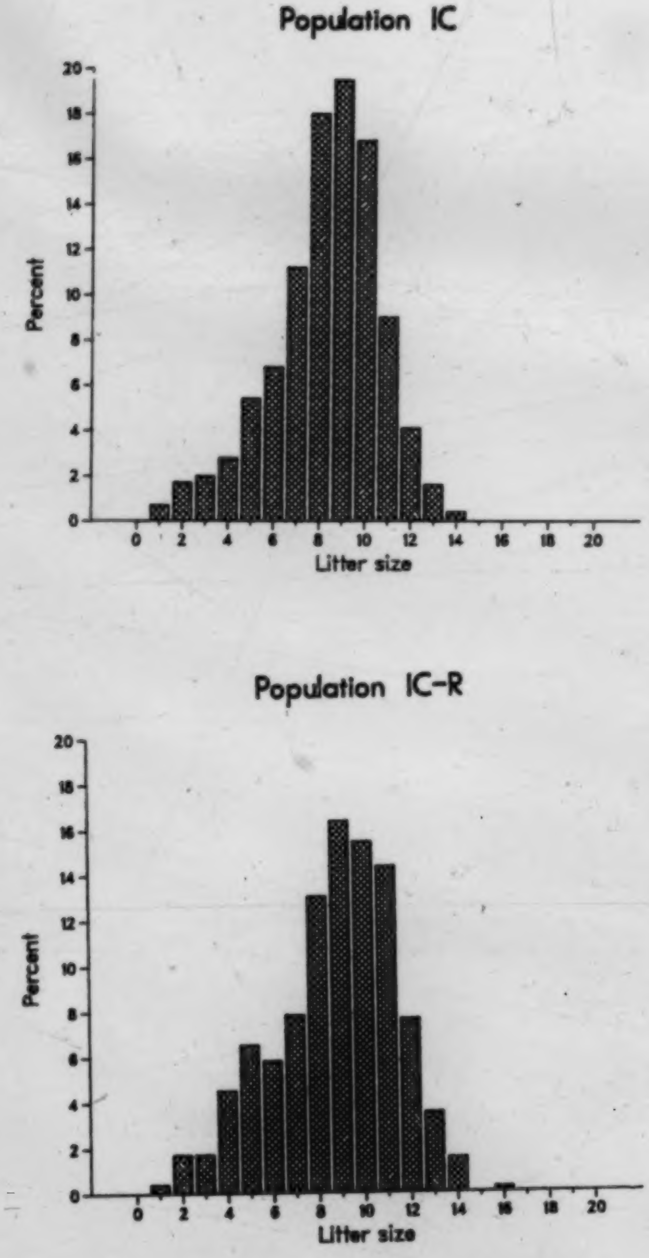


Figure 7. Frequency distributions of litter size in the IC and IC-R populations

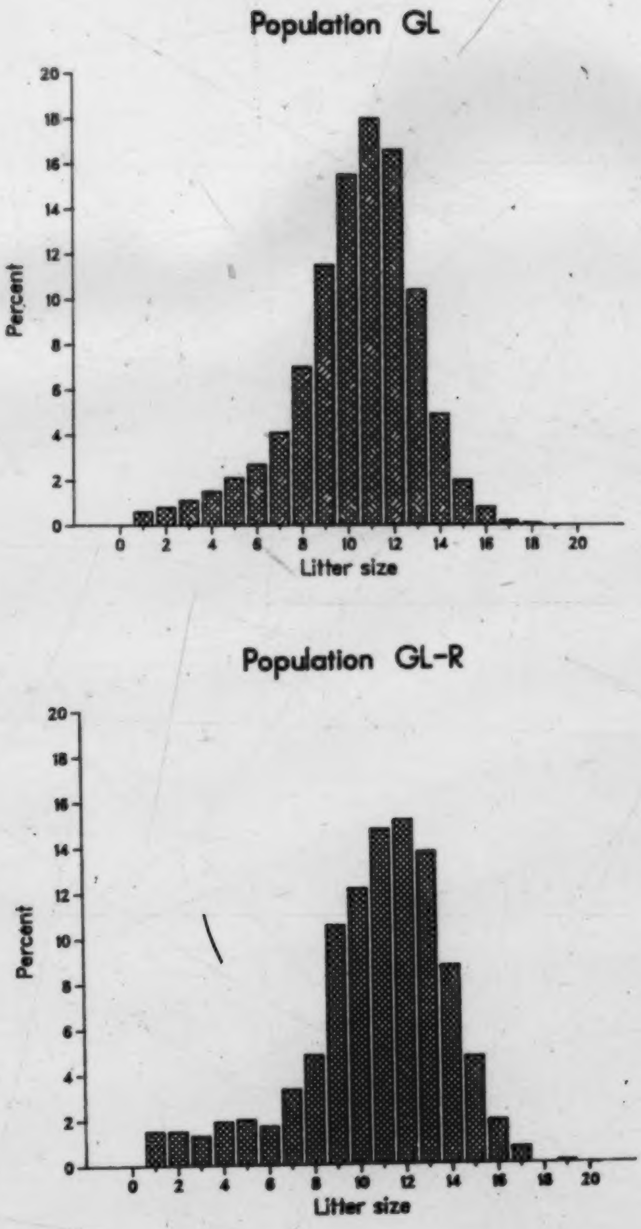


Figure 8. Frequency distributions of litter size in the GL and GL-R populations

APPENDIX VI.1 Plots of mean litter size by generation in different populations

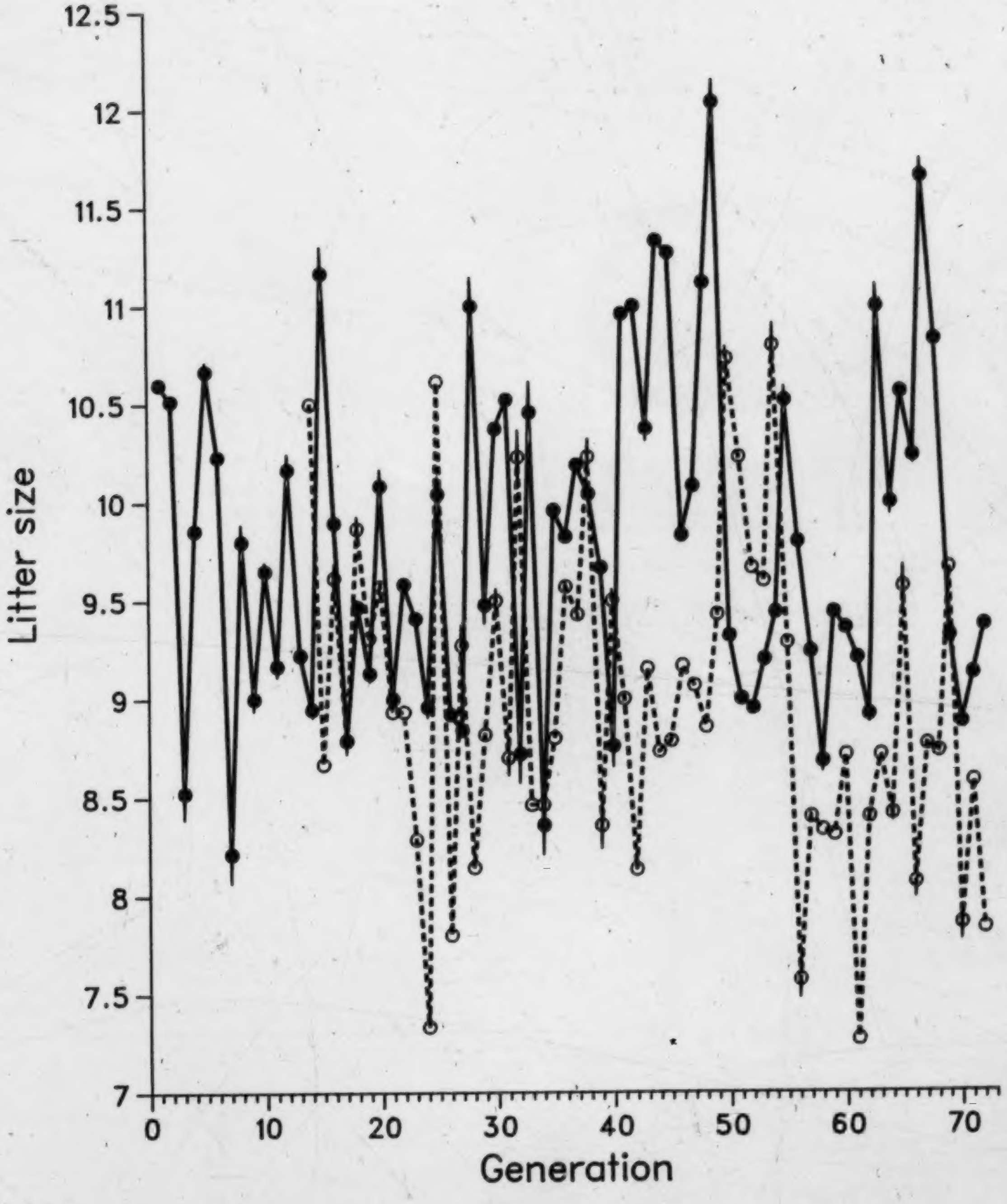


Figure 9. Mean litter size by generation in the QL (solid line) and QL-R (broken line) populations

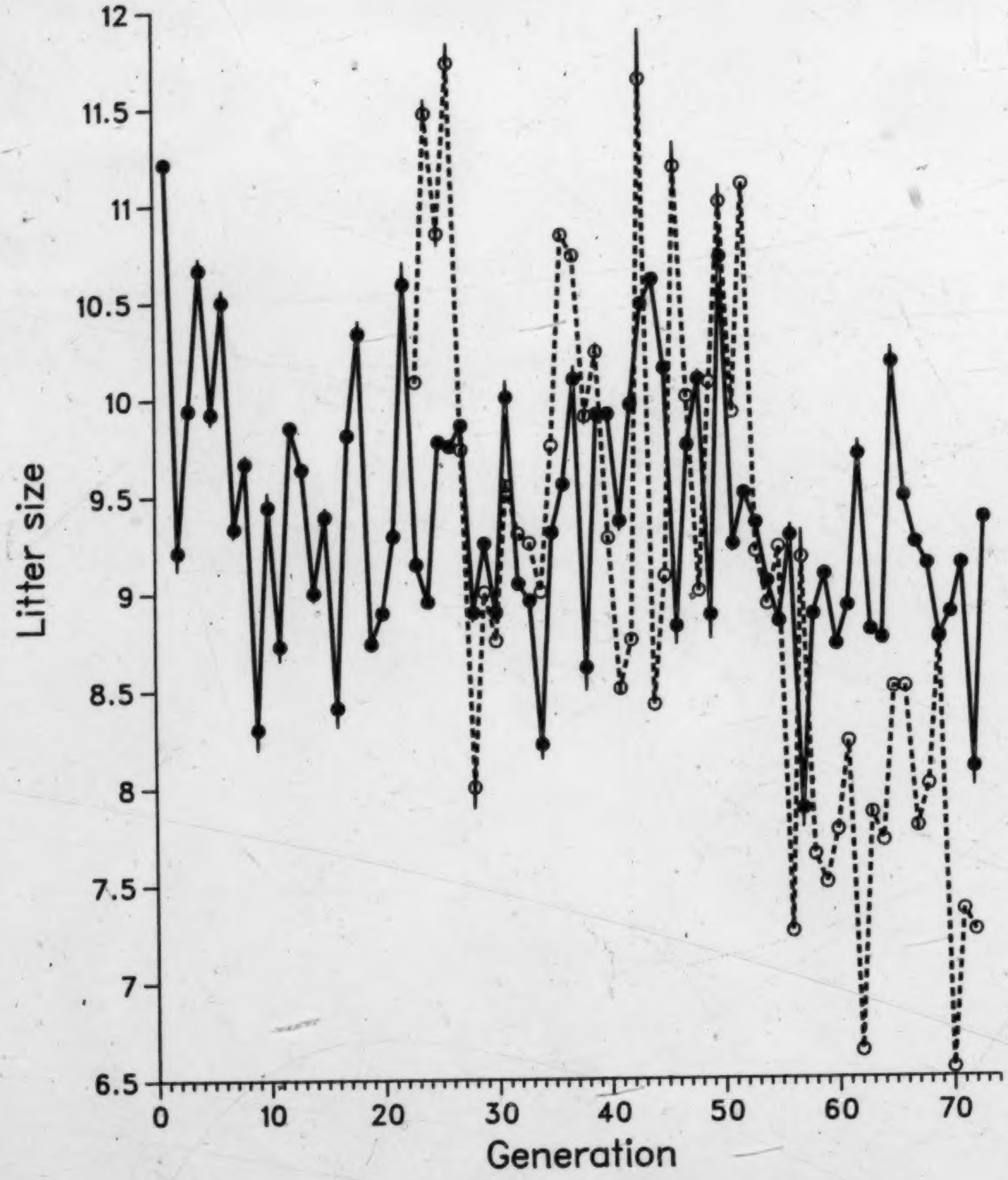


Figure 10. Mean litter size by generation in the LX (solid line) and LX-R (broken line) populations

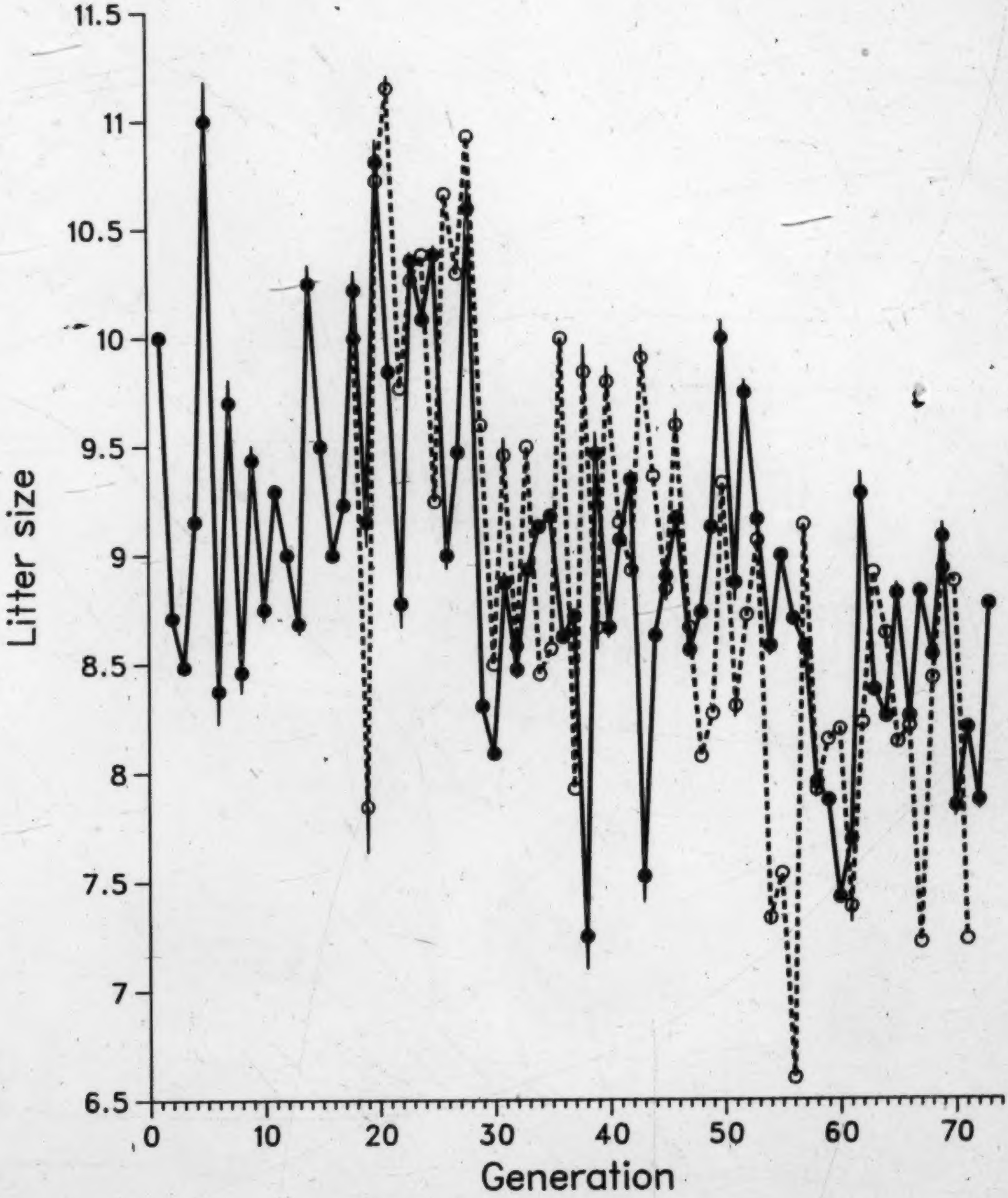


Figure 11. Mean litter size by generation in the NB (solid line) and NB-R (broken line) populations

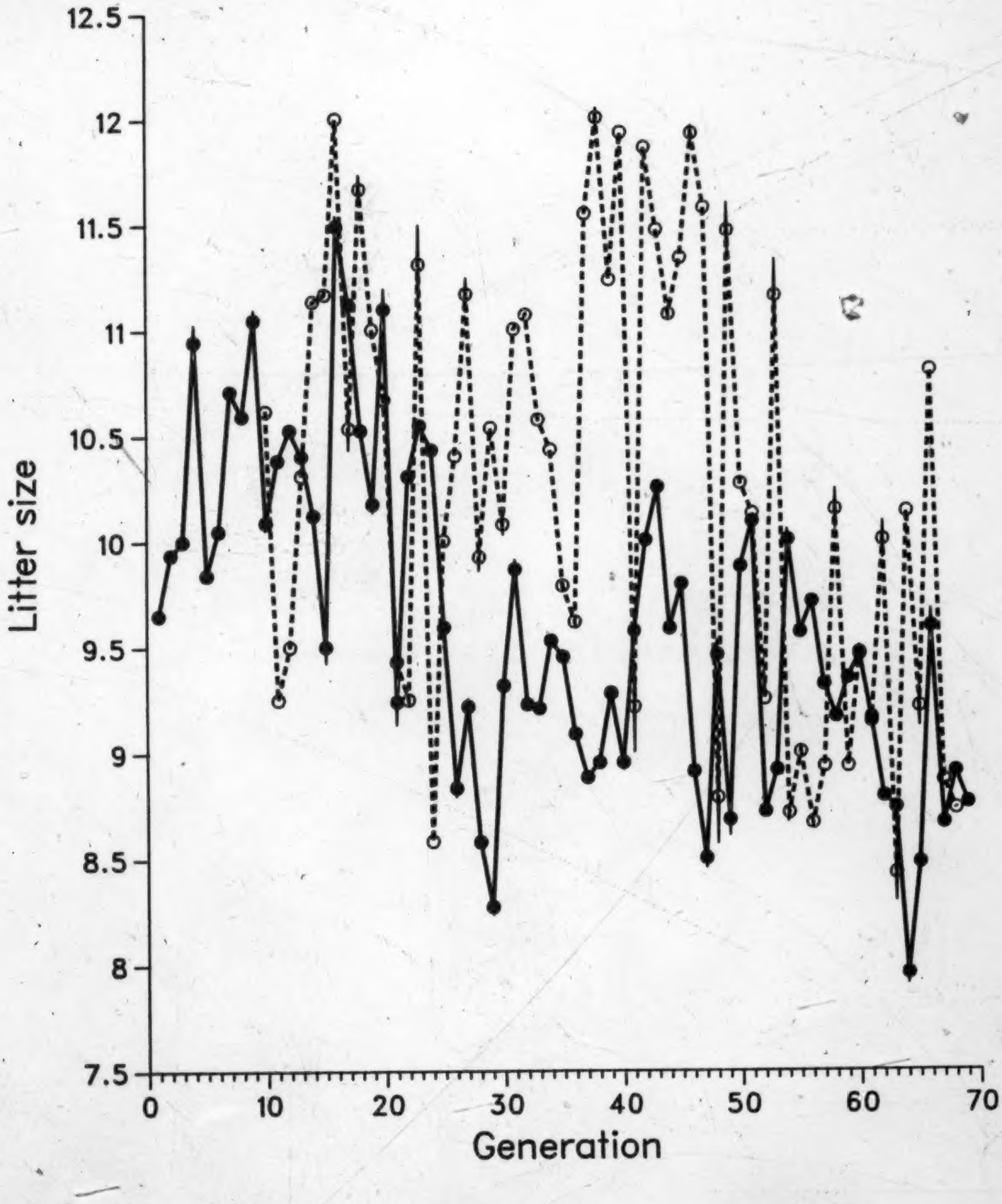


Figure 12. Mean litter size by generation in the OC (solid line) and OC-R (broken line) populations

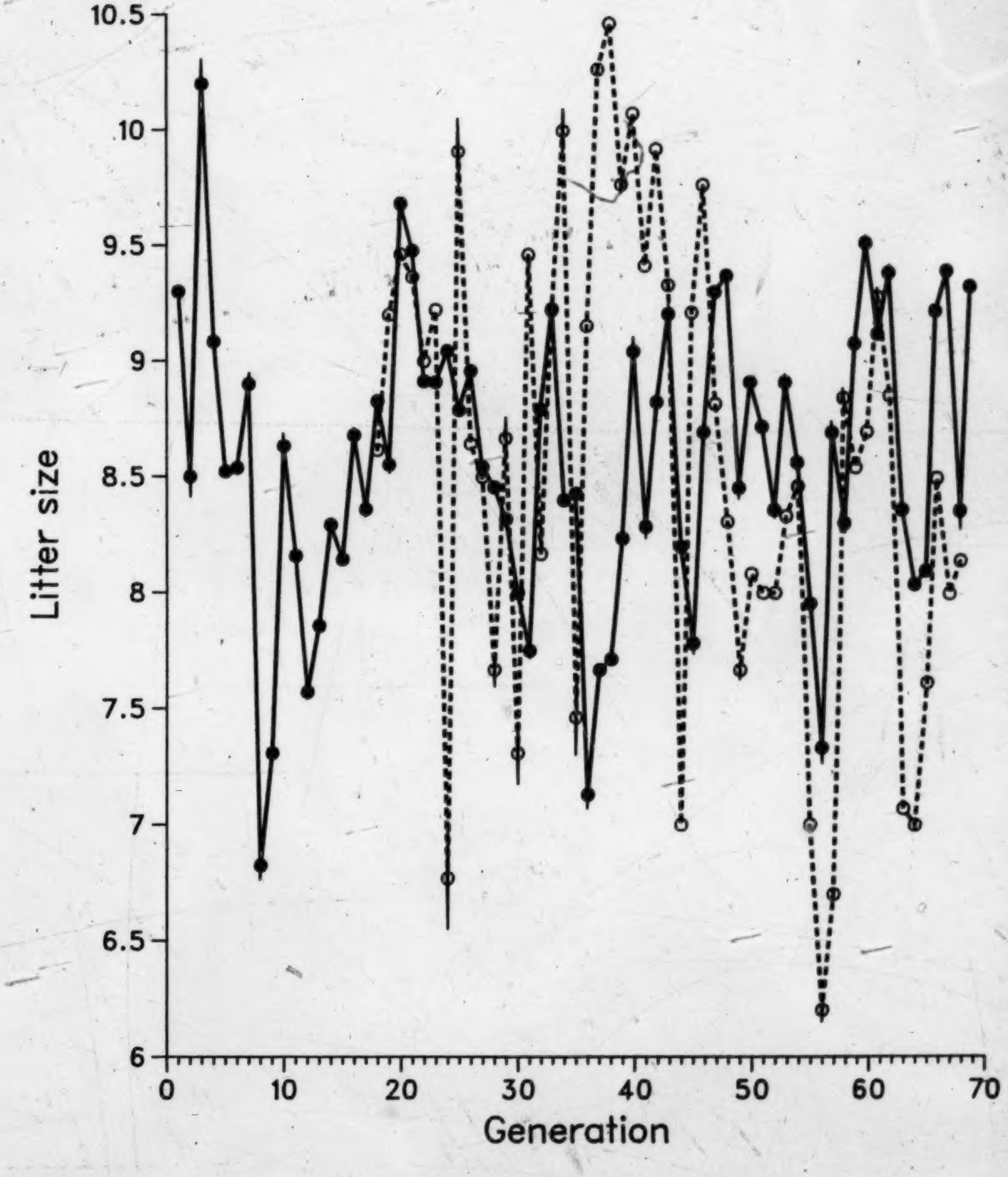


Figure 13. Mean litter size by generation in the AC (solid line) and AC-R (broken line) populations

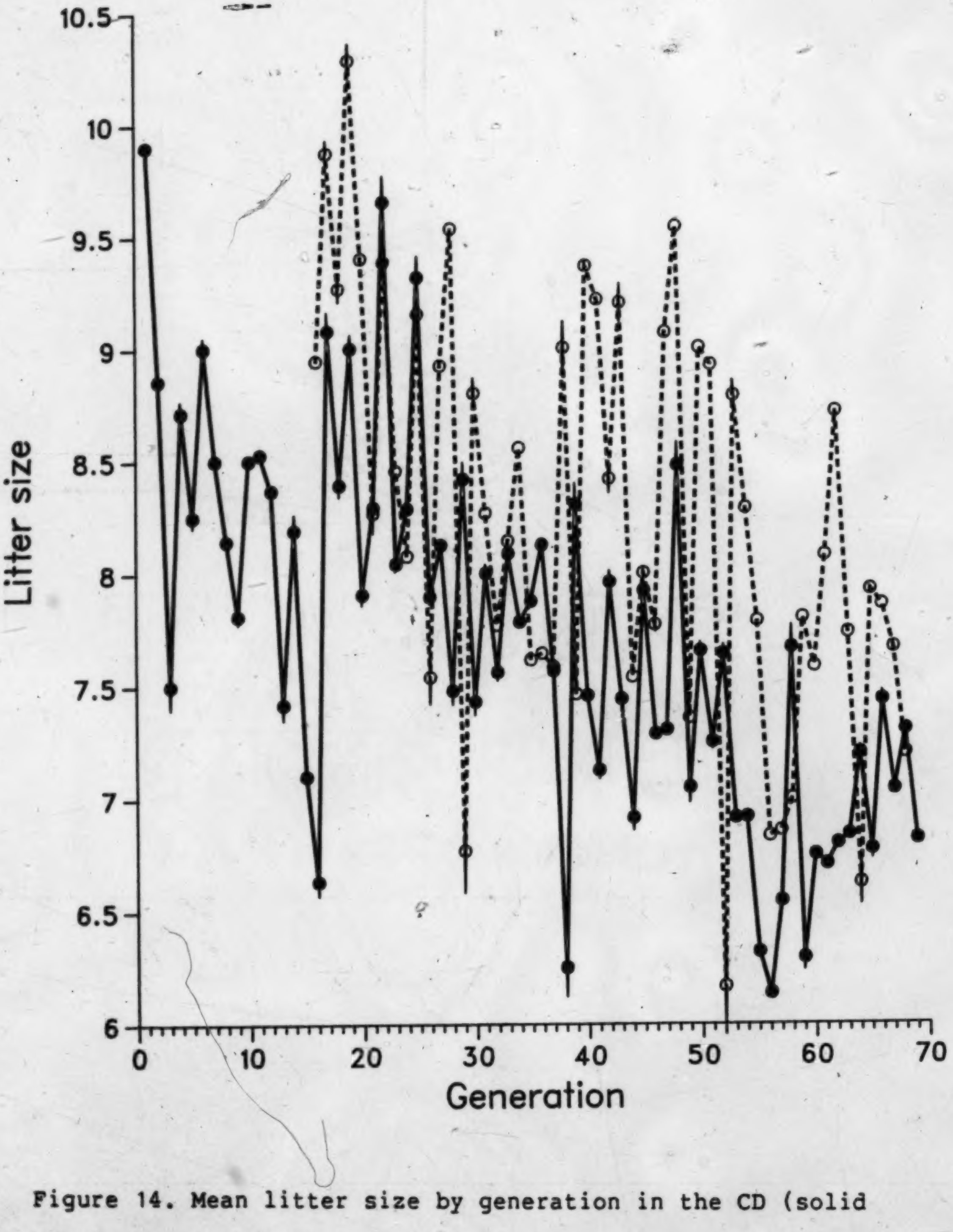


Figure 14. Mean litter size by generation in the CD (solid line) and CD-R (broken line) populations

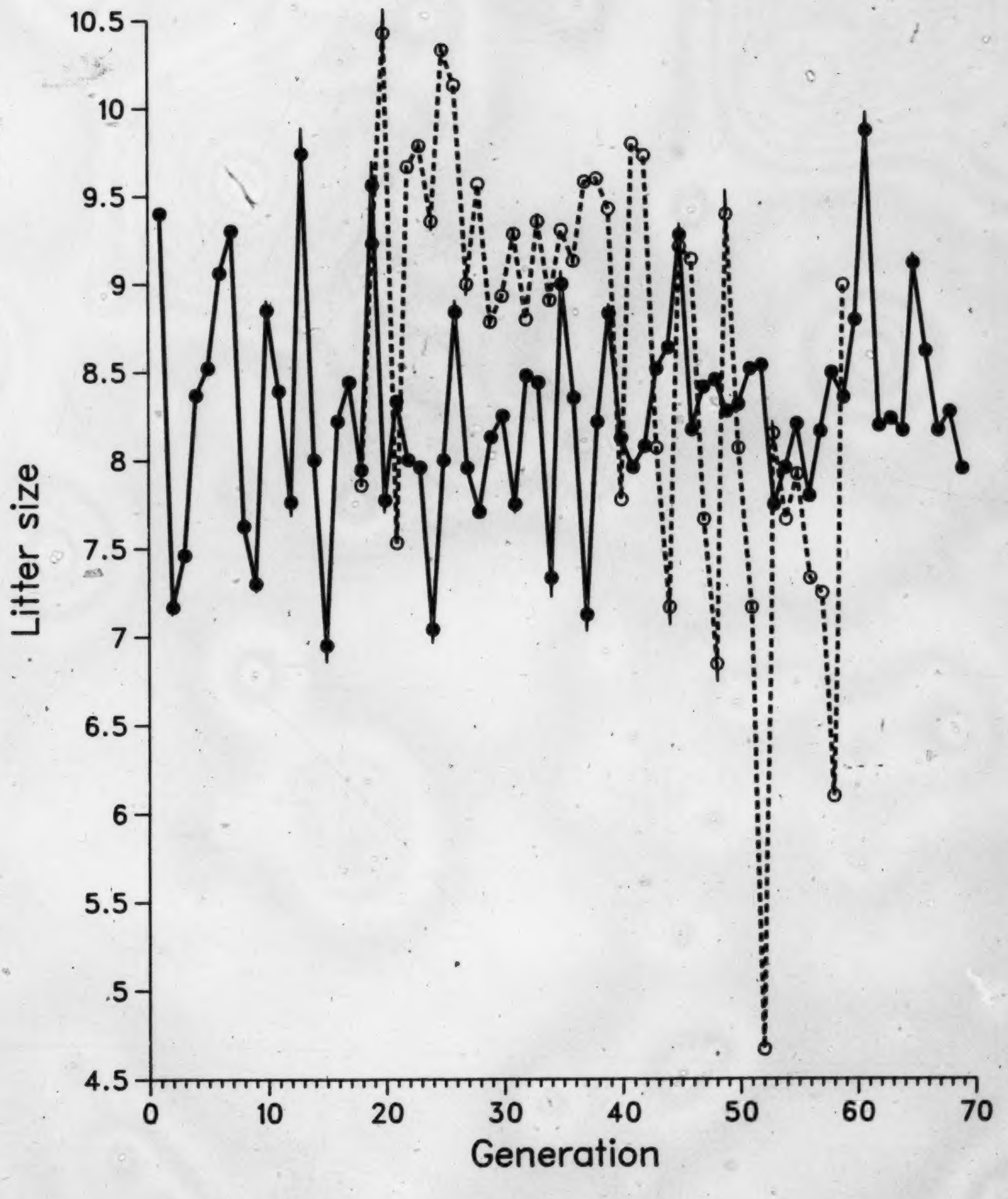


Figure 15. Mean litter size by generation in the IC (solid line) and IC-R (broken line) populations

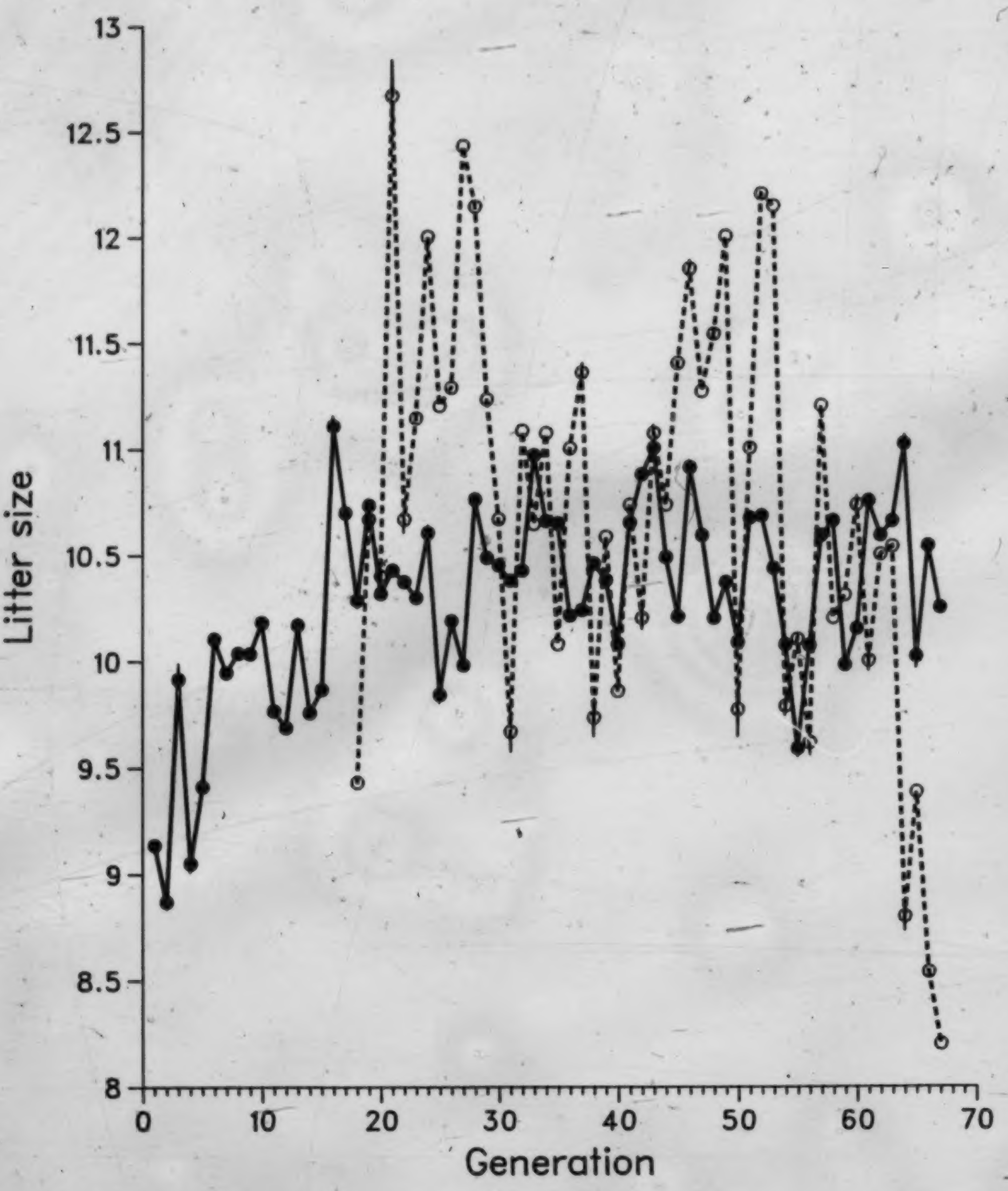


Figure 16. Mean litter size by generation in the GL (solid line) and GL-R (broken line) populations

APPENDIX VI.2 Time Series Analysis

The theoretical aspects of time series analysis, as described by Box and Jenkins (1976), is quite sophisticated, and only a few terminologies which were used in the text will be defined here.

Time series: A time series is a set of observations generated sequentially in time, and is regarded as a realization of a stochastic process, i.e. the phenomenon evolves in time according to probabilistic laws. Time series analysis requires data on only one variable, namely the output of the system, and the main concern of the analysis is to find any time-related pattern by making use of the values of the series itself.

Autocorrelation coefficient: The key statistic in time series analysis is the autocorrelation coefficient, which is the correlation of the time series with itself lagged 1, 2, . . k periods. Theoretically, all autocorrelation coefficients for a series of random numbers must be zero.

Partial autocorrelation coefficient: Partial autocorrelation coefficients are used to measure the degree of association between Y_t and Y_{t-k}, when the effects of other time lags (1, 2, 3, . . k-1) are removed. The concept is similar to partial regression coefficients in regression analysis. The partial autocorrelation coefficient is used as an aid for identification of the appropriate model.

Backward shift operator (B): The backward shift operator is a convenient tool in time series analysis. It shifts the data back one period, as follows:

$$B\ Y_t = Y_{t-1}$$

The following form shifts the data two periods:

$$B(B\ Y_t) = B^2\ Y_t = Y_{t-2}$$

Stationarity: The process is stationary if it remains in equilibrium about a constant mean level. If series is stationary, the autocorrelation coefficients drop to zero after the second or third time lag, while for a nonstationary series they remain significantly different from zero for several time periods. The existence of a trend (linear or nonlinear) in the data suggests that the successive values will be correlated with each other. The autocorrelation coefficients for one time lag will therefore be large, and gradually decrease as time lags increase. The method of differencing is routinely employed to remove the nonstationarity, i.e., by subtracting the consecutive values of the series.

$$Y'_t = Y_t - Y_{t-1} = Y_t(1-B)$$

The autocorrelation coefficients of the new series resulting from the subtraction would drop to zero rapidly if the series became stationary, otherwise the process of subtraction should be continued.

Autoregressive models, AR(m): In this model the current value of the process (Y_t) is expressed as finite, linear aggregate of previous values of the process (Y_{t-1}, Y_{t-2}, etc.) and a random error (ϵ_t).

$$Y_t = \mu + \phi_1 Y_{t-1} + \phi_2 Y_{t-2} + .. + \phi_m Y_{t-m} + \epsilon_t$$

Hence the variable Y_t is regressed on its previous values. In this model, μ is a constant term and ϕ_j is the *j*th autoregressive parameter which takes values between +1 and -1. The simplest form of an autoregressive process is the first order autoregressive model, AR(1), which has the following form:

$$Y_t=\mu+\phi_1 Y_{t-1} +\epsilon_t$$

This model can be written as follows by using the backward shift operator:

$$Y_t-\phi_1 Y_{t-1}=\mu+\epsilon_t$$

$$Y_t(1-\phi_1 B)=\mu+\epsilon_t$$

Moving average models, MA(n): In such models any observed value at time t (Y_t) is linearly dependent on a finite number of previous error terms (ϵ's).

$$Y_t=\mu+\epsilon_t - \theta_1\epsilon_{t-1} - \theta_2\epsilon_{t-2} - . . \theta_n\epsilon_{t-n}$$

In this model, μ is a constant term and θ_j is the *j*th moving average parameter which takes values between +1 and -1. The simplest model of this type is first order moving average model, MA(1), which has the following form:

$$Y_t=\mu+\epsilon_t - \theta_1\epsilon_{t-1}$$

and can be presented in the form of

$$Y_t=\mu+ (1-\theta_1 B)\epsilon_t$$

Autoregressive- integrated- moving- average models, ARIMA(m,d,n): Autoregressive models can be coupled with moving average models to form autoregressive- moving average, or ARMA(m,n) models. When the series become stationary with *d* order differencing, the general type of the time series models called autoregressive- integrated- moving- average models will result. The parameters *m*, *d* and *n* referring to the orders of autoregressive process, differencing and moving average process. For example:

ARIMA(0,0,0) is white noise ($Y_t=\mu+\epsilon_t$)

ARIMA(0,1,0) is $Y_t=Y_{t-1}+\epsilon_t$

ARIMA(1,0,0) is the same as *AR(1)* as described above.

ARIMA(0,0,1) is the same as *MA(1)* as described above.

ARIMA(1,0,1) has the form

$$Y_t=\mu+\phi_1 Y_{t-1}-\theta_1\epsilon_{t-1}+\epsilon_t$$

or

$$Y_t(1-\phi_1 B)=\mu+(1-\theta_1 B)\,\epsilon_t$$

ARIMA(1,1,1) is

$$Y_t(1-B)(1-\phi_1 B)=\mu+(1-\theta_1 B)\,\epsilon_t$$

Seasonality: Seasonality is defined as a pattern that repeats itself over fixed intervals of time (after *k* time lags). If the pattern is consistent, the autocorrelation coefficients of *k* time lags (r_k)will have high positive values, and $r_k > r_{2k} > r_{3k}$, ..., and several of such values are significant. In exactly the same way that consecutive data points may exhibit *AR*, *MA* or mixed *ARIMA* properties, so data separated by a whole season with *k* time lags apart may exhibit the same properties. The *ARIMA* notation can be extended to handle seasonal aspects, with the general form of $ARIMA(m,d,n)(M,D,N)^k$, where *(m,d,n)*are the parameters for the nonseasonal part of the model, *(M,D,N)* are the parameters for the seasonal part, and *k* is the number of periods per season. For example, *ARIMA(1,1,1)(1,1,1)*^{4} model takes the following form :

$$Y_t(1-\phi_1 B)(1-\Phi_1 B^4)(1-B)(1-B^4)= (1-\theta_1 B)(1-\Theta_1 B^4)e_t$$

The terms in this model are:

$(1-\phi_1 B)$ nonseasonal AR(1)

$(1-\Phi_1 B^4)$ seasonal AR(1)

$(1-\theta_1 B)$ nonseasonal MA(1)

$(1-\Theta_1 B^4)$ seasonal MA(1)

(1-B) nonseasonal first difference

$(1-B^4)$ seasonal first difference

Fitting time series models to the data: In analysis of time series, the autocorrelation and partial autocorrelation coefficients for several time lags are examined to see if any of them are significantly different from zero. Based on the sign, pattern and number of significant autocorrelation and partial autocorrelation coefficients the probable models are selected. The process can be summarized as follows:

i-When the autocorrelations suggest nonstationarity (as explained before), first difference should be computed, and the autocorrelations of the resultant series examined. If they are still nonstationary, the process of differencing should be continued to achieve a stationary series. In most practical situations, one or two differencing make the series stationary.

ii-When the stationarity is achieved, any remaining pattern should be examined by looking at the autocorrelation and partial autocorrelation coefficients. There are four possible cases to consider:

a-Series is white noise, which is characterized by no significant autocorrelation or partial autocorrelation coefficients.

b-Nonseasonal AR or MA process.

c-Seasonal AR or MA process.

d-A mixture of seasonal and nonseasonal AR or MA process.

iii- The possible models are identified and fitted to the data. The most appropriate model provides a random residual with no significant autocorrelation coefficient.

It should be noted that the above description is an oversimplification of the time series analysis. There are more statistics which can be used as aids for model identification and fitting. One of such statistics is the Box-Pierce Q statistic which determines whether a set of autocorrelation coefficients, taken as a whole, represents a departure from a null set. Since the aim of this Appendix was to briefly define the terminology which was used in the text, the details of the model identification were left out of the discussion.

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